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AGARD

ADVISORY GROUP FOR AEROSPACE RESEARCH & DEVELOPMENT

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AGARD ADVISORY REPORT 351

Echocardiography in NATO Aircrew — A Multi-national Study

(l'Echocardiographie chez les pilotes de l'OTAN — une étude multinationale)

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NORTH ATLANTIC TREATY ORGANIZATION

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Echocardiography in NATO Aircrew — A Multi-national Study

(AGARD AR-351)

Executive Summary

Based on physiologic considerations and observations in animal experiments, a serious concern was raised: that repeated exposures to increased radial acceleration forces (+Gz) might have a deleterious effect on the pilot's heart. This concern was supported by the results of a preliminary echocardiographic (heart ultrasound) study carried out by French researchers and reported to AGARD in 1985. There were a number of uncontrolled variables in that initial study, including the amount of exercise and smoking. The investigators cautioned against forming any definite conclusion and recommended further studies.

Because of these potentially serious occupational concerns and the findings of the preliminary study, the AGARD Aerospace Medical Panel initiated a carefully controlled study using echocardiography to compare current NATO pilots flying high-sustained G (HSG) aircraft with a control group of transport and rotary wing pilots. HSG aircraft were arbitrarily defined as those designed to maintain greater than +7Gz for at least 15 seconds, e.g. F-15, F-16, F-18, Mirage 2000, Hawk.

Working Group 13 designed a protocol by which investigators from many NATO countries could contribute data to a central database. The study was carried out by Working Group 18 and involved over 30 investigators from 13 NATO countries. Data were collected and transmitted for analysis and quality control to a central database at the USAF Armstrong Laboratory at Brooks Air Force Base, Texas.

Over 1600 echocardiograms were entered into the database. Data analyses compared 289 pilots of high sustained G (HSG) aircraft with 254 control pilots.

The results conclusively show that there is no effect of HSG flight on the heart.

The conclusions are limited to the resolution of the technology employed (echocardiography) and to the flight envelopes utilized in the current generation of NATO HSG fighter aircraft.

The study serves as a model by which other military occupational medical questions may be addressed quickly and efficiently by the AGARD Aerospace Medical Panel.

L'échocardiographie chez les pilotes de l'OTAN — une étude multinationale

(AGARD AR-351)

Synthèse

Basé sur les observations et les considérations physiologiques consécutive aux études expérimentales faites sur des animaux exposés à des accélérations radiales répétées (+Gz) et les conséquences délétères possibles pour le cœur du pilote, une inquiétude est née concernant ce sujet au sein de la communauté des médecins de l'air. Cette inquiétude a été confirmée par les résultats d'une étude échocardiographique préliminaire réalisée par une équipe de chercheurs français et publiée par l'AGARD en 1985. L'étude initiale a tenu compte d'un certain nombre de variables non-contrôlés et notamment l'exercice physique et le tabac. Les auteurs ont mis en garde contre tout jugement définitif sur la question et ils ont recommandé de poursuivre les études.

Pour répondre à ces préoccupations professionnelles dues aux conclusions alarmantes de l'étude préliminaire, le Panel de médecine aérospatiale de l'AGARD a lancé une étude échocardiographique, réalisée dans des conditions rigoureusement contrôlées, afin de comparer les résultats obtenus sur un groupe de pilotes d'avions de combat soumis à des facteurs de charge élevés et soutenus (HSG) avec ceux obtenus sur un groupe témoin composé de pilotes d'avions de transport et d'aéronefs à voilure tournante. Les aéronefs HSG ont été définis arbitrairement comme des aéronefs conçus pour maintenir des accélérations supérieures à +7GZ pendant plus de 15 secondes, par exemple le F-15, le F-16, le F-18, le Mirage 2000 et le Hawk.

Le groupe de travail N° 13 a élaboré un protocole pour permettre aux chercheurs des différents pays de l'OTAN de participer à la création d'une base de données centrale. L'étude, qui a été réalisée par le groupe de travail N° 18, a bénéficié de la participation d'une trentaine de chercheurs de 13 pays de l'OTAN. Les données ont été collectées et transmises pour analyse et contrôle de qualité à la base de données centrale établie au laboratoire Armstrong du Brooks Air Force Base, Texas, USA.

Plus de 1600 échocardiogrammes ont été entrés dans la base de données. Les analyses des données ont permis de comparer les 289 pilotes d'aéronefs à facteurs de charge élevés et soutenus (HSG) au groupe témoin de 254 pilotes.

Les résultats montrent très clairement que le vol HSG n'a aucun effet sur le cœur.

Les conclusions se limitent aux possibilités de la technologie mise en œuvre (l'échocardiographie), et aux domaines de vol de la présente génération d'avions de combat HSG de l'OTAN.

Cette étude doit servir de modèle pour l'examen rapide et efficace par le Panel AGARD de médecine aérospatiale d'autres questions touchant la médecine professionnelle.

Contents

Preface

The effects of repetitive high sustained +Gz (HSG) on the human organism have been raised as an occupational medicine issue with respect to the heart, axial spine, and vestibular systems. AGARD AMP Working Group 18 (and its predecessor, WG 13) have addressed the cardiac issue from an echocardiographic standpoint.

This study was conducted as a cross-sectional study, with the dominant variables being those most likely to be affected by HSG. It is possible, of course, that differences may have been found in parameters not investigated. However, a complete echocardiographic study of all possible parameters, of adequate statistical power, after adjusting for multiple comparisons, would have entailed a sample size of prohibitive proportions. A relatively large sample size was required to evaluate even the restricted number of variables in this study. The necessarily focused nature of this study must be kept in mind when interpreting the results. The results demonstrate that no significant echocardiographic differences were found in the hearts of HSG pilots when compared to their counterparts in non-HSG aircraft. We conclude that any possible pathological changes or functional impairments are below the threshold of current ultrasound technology. Subtle changes detectable by such modalities as positron emission tomography or magnetic resonance cannot be excluded. Current echo data do not suggest the need for such studies.

Should a long-term longitudinal echo study of young pilots, looking for +Gz related endpoints, be undertaken? The expense, bayesian issues, observational difficulties, and imponderables of prospective studies to discover unidentified effects must be considered. Based upon the findings of this NATO echo study, the cross-sectional data do not suggest the need for a longitudinal study. Since a great deal of co-factor information has been gathered on the subjects in the NATO echo study, it does seem important to maintain some type of outcome file on the study subjects, where national policy and circumstances allow.

This study involved pilots who used anti-G devices and strategies which were essentially common among the NATO Air Forces. The findings cannot be extrapolated to aircrew utilizing full-body coverage and/or positive pressure breathing devices. Subjects using such devices are exposed to +Gz levels beyond the usual HSG pilot in this study. Further, the devices may impose an additional functional variable, aside from enhanced +Gz performances. Further, the results of this study do not apply to future weapons systems or future life support devices.

This study also served as a template for one methodology to study possible HSG effects. No single NATO Air Force had a denominator large enough to study the echocardiographic issues. Some Air Forces, such as the USAF, had large numbers of aircrew echocardiograms done for aeromedical indications, often with normal concomitant invasive studies. However, because of exclusion criteria, such studies could not be included in the data set. Surveillance echocardiograms from volunteers were included in the data base. The nation members of this study adhered to a common echocardiographic protocol, as well as to an experimental protocol devised by the working group. Variables such as flying exposure and physical exercise were intensively studied. The use of discs to forward data to a central data processing facility, and the adoption of a detailed quality control approach, were strengths of the study, which can be translated to other multi-national studies. Lastly, the investigators summarize the lessons learned in the conduct of technically demanding multi-national studies.

Foreword

AGARD Working Group 18 executed the extensive echocardiographic protocol produced by Working Group 13 in 1990 (AGARD Advisory Report 297).

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ECHOCARDIOGRAPHY IN NATO AIRCREW REPORT OF A MULTINATIONAL ECHOCARDIOGRAPHY STUDY BY AGARD WORKING GROUP 18

INTRODUCTION

In health, the human cardiovascular system operates in Earth's gravitational field (+1g) with great efficiency. During abrupt changes of posture, rest and exertion, and during metabolic demands, circulatory perfusion of all organs and systems is maintained, adequately if not optimally. Modern high-performance military aircraft flight imposes massive and unprecedented gravito-inertial forces on the circulatory system, which shows remarkable ability to adapt acutely to these unfamiliar stressors. That there are limits to this cardiovascular adaptability was, however, realised early in the history of military combat flying (Ref 1). High positive G forces (+Gz) would induce visual loss (grey-out), soon followed by loss of consciousness (LOC, blackout) due to cerebral ischemia. Trained pilots could counter these effects by straining manoeuvres, but ultimately high enough +Gz would defeat these efforts. A large part of aviation medical research over many years has been devoted to finding ways of increasing the pilot's G-tolerance and thus his ability to fly ever more powerful and agile interceptor aircraft (Ref 2). However, even with modern counter-pressure garments, tilt-back seats and positive pressure breathing, there are limits to human tolerance of +Gz. Though consciousness may be retained at up to +12 Gz, other systems, notably the pulmonary (Ref 13) and musculo-skeletal systems, limit significant progress beyond this point.

The acute effects of high G-forces include extreme deformation of soft tissues including the heart, great vessels and other mediastinal structures (Ref 3). These effects are rapidly reversed with the off-set of G-forces. In animal studies, subendocardial petechiae have been observed in miniature swine following exposure to very high G-forces (Ref 4,5), though this effect may have been attributable, at least in part, to catecholamine secretion due to the stress of handling and restraint (Ref 14). Whether there are any long-term effects from such cardiac lesions is unknown. However, animals subjected to repeated acceleration over six months showed suggestive evidence of myocardial scar-tissue (Ref 15). Isolated clinical cardiac mishaps have occurred during high performance flight, but there has been no apparent evidence of delayed or long-term ill-effects in humans attributable to acceleration stresses. Post mortem studies of the hearts of aviators killed in flying or other accidents have at times shown a spectrum of disease types, but there has been no evidence to link pathological process with the type of flying experience. It has been generally accepted that there is complete and immediate recovery from the physical effects of increased G-forces, and that a pilot's tolerance of repeated G-stress is limited only by fatigue.

In 1985, a preliminary report from the Centre Principal d'Expertise Medicale du Personnel Navigant de l'Aeronautique (CPEMPN), France (Ref 6), reported that there was an increase in the size of the right ventricle in the pilots of Mirage 2000 (fast jet) aircraft, when they were compared with pilots of other (non high-performance) aircraft. A subsequent report from Belgium (Ref 7) failed to confirm any such difference. The Aerospace Medical Panel of AGARD (Advisory Group for Aerospace Research and Development) decided that the matter required further enquiry. A Working Group (AGARD WG 13) was established to investigate and advise on the optimum method of studying pilots' hearts by echocardiography. The inaugural meeting was convened in May 1988 and the Working Group reported in 1990 (Ref 8). The report provided a protocol for the echocardiographic examination of military pilots serving in NATO air forces, and also made detailed proposals for a multi-national study designed to detect any effect of high-performance flight on pilots' hearts. The report covered subject selection, exclusion criteria, recording of potentially confounding variables or co-factors, technical details of echocardiographic recording, and a unique software documentation package "PILOTES" (M Bertrand Piedecoq, France). Details of data work sheets, flow sheets, consent forms, definitions and quality control were also provided.

After considering the WG 13 report, the Aerospace Medical Panel of AGARD inaugurated a new Working Group 18 (WG 18), charged with carrying out the research necessary to affirm or refute the suggestion that the stresses of high performance flight had a detectable effect on

pilots' hearts. This paper reports the results of that research.

METHODS

An early decision was made to limit selection to pilots rather than to aircrew generally. Differences in education, training, qualifications and experience between pilots and other aircrew might introduce unquantifiable, but potentially important confounding effects. Pilots greatly outnumber other aircrew (navigators, systems operators) in high performance flying, whilst the reverse is true in transport-type aircraft. At the inception of the study there were still very few qualified women pilots in NATO air forces, and the decision was therefore taken to study only male pilots.

The Working Group planned two types of study. The first would be cross-sectional, a "snapshot" at a single moment in time, and would be composed of single examinations of trained pilots. All must be graduate pilots (ie, have been awarded their flying wings) and be on current flying status, that is, be engaged on a flying tour or be eligible for flying duties. If otherwise employed at present (eg in a staff appointment) they must have flown actively within the previous three years.

The second type of study contemplated was a longitudinal study involving an initial echocardiogram at, or very soon after, entry into flying training. These pilots would be followed up at two or three-yearly intervals to record the effects, if any, of cumulative flying stresses over time. So far, very few subjects have been recruited for the longitudinal study, and no data on this part of our work will be presented here. An open issue is whether a longitudinal study should be undertaken if the cross-sectional study is unrevealing.

STUDY DESIGN

Pilot subjects for the cross-sectional study were to be recruited by two methods, prospective and retrospective. Prospective echocardiographic studies were obtained by several means. In some countries, echocardiography is performed as a part of the periodic flight physical examination. In other countries, volunteers were solicited during flight physicals, during G-training programs, or during special visits to flying stations. The second method, retrospective, was theoretically made possible by the fact that a number of air forces had routinely carried out echocardiography on their aircrew over several previous years. These historical echocardiograms on healthy pilots could be used, provided their technical quality was adequate, that a number of requisite measurements had, or could be made on them, and that adequate physiological and other details of the pilots concerned were available, as well as a complete flying history. Ultimately, virtually all retrospective studies which were scrutinized for possible entry into the study were discarded, owing to the stringent protocol requirements regarding echocardiographic data, flying history and cofactor data. Since all of the retrospective studies were, by definition, performed prior to protocol publication, it is not surprising that virtually all retrospective studies were excluded. Large numbers of echocardiograms had also been performed in several Air Forces on pilots undergoing clinical or aeromedical evaluations to determine fitness to fly. Although many of these echocardiographic examinations were performed in asymptomatic pilots with completely normal cardiovascular systems (as determined by current technology, including normal left heart catheterization), no subjects were enrolled in the study whose echocardiograms had been performed for any clinical or specific aeromedical indication. Only surveillance echocardiograms or echocardiograms performed specifically for this study were deemed usable by the Working Group.

EXCLUSION CRITERIA FOR CROSS-SECTIONAL ECHO STUDY

1. Known pre-existing cardiovascular disease.
2. Referral for suspected cardiovascular disease.
3. Cardiovascular drugs (lipid-lowering agents excepted).
4. Pulmonary disease.
5. Female sex.
6. Unavailable flying history.
7. Unavailable exercise history (any type).
8. Unacceptable echo quality.
9. Outside age limits (under 18 or over 55).
10. Concurrent high-performance and transport flying.
11. No flying experience in previous 36 months.

In practice, inadequate echo quality or incomplete data proved reasons for exclusion in only a minority of studies, nearly all retrospective.

Originally, we had expected that military pilots would be fairly easily classifiable into two groups: (1) fighter pilots, regularly and frequently experiencing high sustained G-forces (HSG); and

(2) non-fighter pilots, (tanker-bomber-transport) experiencing "straight and level" flying at one G, almost exclusively. Using this simple classification, it should be easy to identify pairs of pilots, well matched in all important characteristics apart from flying experience (HSG vs non-HSG). Very early in the study, however, we became aware that this simple classification did not hold for a large number of subjects. We knew, of course, that all military pilots are exposed to some HSG flying during training. However, some pilots had spent several years flying high-performance aircraft and then changed to non-HSG flight. These pilots with "mixed" flying histories must clearly be classified separately from "pure" HSG and "pure" non-HSG pilots.

Further potential difficulties arose from consideration of aircraft types, of which we identified well over 100 in the NATO inventory. Many "fast jets", such as the multi-national Tornado, are produced in various versions for specialised roles, some of which entail little if any HSG. Many missions, even in pure fighter aircraft (eg, air to air interceptor) may involve little if any HSG. Some "fast jets" are used exclusively for reconnaissance or aerial photography involving "straight and level" flying nearly all the time. Metal fatigue and other wear and tear phenomena can be delayed by restricting an aircraft's exposure to high acceleration forces. Some air forces economise by imposing such restrictions during training flights. Changes in the doctrine of air warfare, and the introduction of novel weapons systems and flying manoeuvres, as well as advanced life support systems , may greatly alter the pattern of military flying.

There are no generally accepted definitions of what constitutes high sustained G, or high performance flight, or even a fast jet. Some piston-propeller aircraft (display and training machines) can develop G-forces comparable with those of many fast jet aircraft -indeed, qualified flying instructors probably experience more G-forces than most other pilots. Faced with these difficulties, we adopted an arbitrary classification of aircraft and of pilots.

Type A (HSG) aircraft are those designed to be capable of sustaining turns at greater than 7Gz for more than 15 seconds. Examples include the Mirage 2000, F15, F16 and Hawk aircraft.

Type B aircraft are fighter, bomber or trainer aircraft, nearly all jet-engined, capable of high performance flight but of lesser degree than Type A (HSG) aircraft. Type B aircraft include the F4, F111 and A10. The latest type of attack helicopters are also included.

Type C aircraft comprise transport, patrol, tanker, early warning and similar aircraft deployed essentially in "straight and level" flying, and all "conventional" helicopters.

See Annex (D)

We classified pilots into five categories:

> XX pilots have flown Type A (HSG) aircraft for 75% or more of their flying hours since completing flying training.
>
> YY pilots have flown Type B aircraft for 75% or more of their flying hours since completing flying training.
>
> ZZ pilots have flown Type C aircraft for 75% or more of their flying hours since completing flying training.
>
> AB pilots have had a mixed flying career, 75% or more in Type A and Type B aircraft, but with an insufficient percentage of hours in either type to qualify for XX or YY classification.
>
> NN pilots comprised any remaining study subjects.

We attempted to exclude the possible confounding effect of varied initial flying experience by subtracting the known hours of flying training from the total flying time recorded. Where flying training duration was unknown or not recorded, a total of three hundred hours was assumed. Hence, each pilot's total flying hours recorded in this report have been reduced by his actual hours in flying training, if known, or by three hundred hours, when his training duration was unknown or uncertain.

PROTOCOL

A standard questionnaire was completed by each subject; immediate help from the investigators was available in case of difficulty, misunderstanding or perceived ambiguity of questions. The questionnaire is shown at Annex A. Questions were addressed particularly to a detailed flying history (pilots were encouraged to bring their log books for reference), especially regarding the number of hours flown in the three

main aircraft types. The subject's exercise habits, past and present, were considered a particularly important co-factor, and two types of exercise history were obtained. The first was essentially qualitative and was divided into aerobic and isometric, each category being sub-divided by arbitrary criteria into four levels, ranging from sedentary to regular and heavy. (This type of exercise history -Type I - had by definition to be available for all subjects including those recruited retrospectively). The second type of exercise history - Type II - was obtained only from subjects recruited prospectively. It consisted of a very detailed history enquiring specifically for participation in thirty-four sports or other potentially vigorous forms of physical activity, many of these being sub-divided by intensity, eg endurance running (jogging) at various speeds ranging from 5.5 to 11 m.p.h. The subjects estimated the amount of the various forms of exercise taken per day, the number of days per week on which each exercise was taken, and the regularity of each exercise over the previous six months. Given the subject's height and body weight it was possible to calculate his exercise energy expenditure using standard tables (Ref 10, 11) and then compute his total average weekly energy expenditure in Kilo-Joules over the past six months. A detailed life-time history of tobacco-smoking was also obtained, and recorded as a total of pack-years (one pack contains 20 cigarettes. If a pilot had smoked 1.5 packs/day for 10 years and then 1 pack per day for the next 10 years, that would be a 25 pack-year history). Six cigarillos, 3 cigars or 3 bowls of pipe tobacco were equivalent to one pack of cigarettes. The same information from ex-smokers was supplemented by a note of the time interval in years since quitting.

Physical examination was limited to height (in socks), weight (in light indoor clothes without shoes) and blood pressure, recorded sphygmomanometrically, seated and supine. Blood total cholesterol and HDL cholesterol (fasting values) were recorded for most subjects.

Each subject was awarded a unique alphanumeric identifier which included a National code and a serial subject number; other data (eg base location) could be included at the discretion of individual investigators. The names of individual subjects were omitted from all study documents, and nominal rolls were not maintained. No central roll of names existed, nor did a master roll exist at the central database facility. This system ensured the anonymity of subjects.

ECHOCARDIOGRAPHIC STUDY

Echocardiography was carried out using standard techniques and positions (Ref 9). Although equipment varied between Nations, all prospective studies (and most retrospective) were carried out using modern 2-D machines, mostly equipped with continuous, pulsed wave and colour Doppler. Annex B shows the work sheet with the measurements and observations required. Two measurements from the apical four-chamber view (maximum [transverse] right ventricular internal dimension, and right ventricular area, items 43 and 44) are rarely made in clinical practice.

Annex C indicates how these measurements were obtained, at the appropriate stage of the cardiac cycle by ECG reference, probe angle being adjusted to optimise the measurements.

Although attempts were made to quantify mitral and tricuspid valvular regurgitation in percentage terms, it was accepted that estimates of the magnitude of regurgitation were to some extent subjective. Minor degrees of insufficiency of the mitral, pulmonary and tricuspid valves are known to be commonplace in healthy subjects (Ref 12). Accordingly we reported only moderate or severe insufficiency of these valves. At the aortic valve, absolutely minimal (often "uncertain" or arguable) insufficiency was ignored; mild, moderate or severe regurgitation being recorded. Prolapse of mitral and tricuspid valves was classified as absent or present.

All prospective studies were recorded on video tape, and chart recorders were used to obtain hard copy for manual measurements, eg of E-F slope and flow velocity. Wherever possible, however, measurements were made by electronic calipers at the time of the study. Data were recorded on a standard work sheet and transferred to disc using the programme referred to above.

Quality Control (QC) was judged to be of particular importance because the study was based on a single technology (echocardiography) of fairly recent introduction and known critical dependence on individual operator skills. We considered several sources of variability or error. Intra-operator variability would be inevitable, based on the limitations of human accuracy in measurement. It seemed possible this type of error might vary appreciably between observers, based on individual experience of echocardiography and other factors. Errors of the

method might arise from the fact that echocardiographic images, irrespective of operator skills, vary greatly in quality between individual subjects. Definition, of chamber walls for example, may be uncertain. In these circumstances, the apparent precision of electronic measurement, to several decimal points, may be misleading. Within subject variability might arise from alterations in certain dynamic measurements such as beat-to-beat variability of mitral valve movement. Information on the extent of such short-term variability, and possible longer-term variability due to physiological factors (eg exercise, arousal, hydration, diurnal factors etc) is generally lacking. Lastly, local practice or technical factors might lead to systematic Inter-operator or between nation variability which could only be detected by retrospective review. We decided to include country of origin as an independent co-variate in our data analysis.

Quality control was planned as a continuous process from the outset of the investigation. QC was to be centralised at the USAFSAM data base. Retrospective QC would be carried out on 5% of randomly selected existing echo studies, provided a full videotape recording was available. Prospective QC would be carried out on 5% of randomly selected echo studies, notably for acceptability of recording quality and accuracy of measurements. The same studies were to be subjected to re-measurement by the data base staff, enabling estimates of inter and intra observer variation in measurement precision. Individual operators would submit 5% of subjects to a duplicate echo examination on the same or the next day, allowing measurements of within-subject or physiological variability (Ref 8).

During preparation of the Technical Section of the report, there was extensive discussion of all aspects of technique and methodology of measurements. Full agreement was reached on all technical aspects. Practical demonstrations of echo examinations were given at USAFSAM and elsewhere, with emphasis on potential pitfalls. A training video was prepared and distributed to all participants, providing precise instructions for all measurements. Initially submitted material from all countries was subject to careful scrutiny and detailed critique. These steps undoubtedly contributed to substantial between-Nation uniformity of technique.

Unfortunately, for various reasons, most notably staff changes, it was not possible to maintain continuous centralised QC throughout the whole duration of the study. However, the following measures were taken: Intra-operator variability was assessed by individual operators selecting 5% of their studies and blindly re-making all measurements. Within-subject (physiological) variability was assessed by duplicate studies on 5% of subjects at up to 24-hour intervals. Inter-operator variability was tested by having a single observer at the data base select randomly either 5% or ten studies, whichever was the greater, of all studies submitted by each nation. Recorded caliper measurements were erased and all measurements repeated blindly. This also provided evidence of any systematic between-Nation differences. Errors of the method could not be measured numerically, but the few studies found to be technically inadequate were rejected from further analysis.

Intra-operator, inter-operator, and within subject variability were assessed by a simple comparison of the paired measurements obtained. Variability of up to 25% in wall thickness measurements and of up to 10% in all other measurements was considered acceptable. Pairs of measurements differing by more than these amounts were noted and the results expressed as percentages of the total number of measurements made.

STATISTICAL METHODS.

We considered various approaches to the statistical management of our data. At first, when we believed that most subjects would be classified either as fast jet or transport type pilots (Type XX or Type ZZ), we hoped to assemble matched pairs of pilots who would be comparable in important characteristics apart from their contrasting flying histories. In practice, a valid sample size of such paired categories was unobtainable. Data were evaluated by "T" tests for unadjusted comparisons, and analyses of covariance for adjusted comparisons. Resampling techniques were used to adjust covariance P-values for multiple testing.

A second approach was made possible by the detailed information on flying history available for all subjects. This allowed an estimation of numbers of hours of experience of high G-forces and allowed rank-ordering of pilots in terms of experience of G stress. This attribute could then be regressed against individual echocardiographic measurements to assess correlations which, if strong, might support the concept of a "dose effect" from cumulative G stress. The influence of potentially confounding variables (co-factors),

such as age or exercise, could again be assessed using this model.

A problem inherent in multiple comparisons was the possibility that apparently "significant" associations might arise by chance. Our hypothesis is that "there is no difference in cardiac chamber dimensions, wall thickness, or echocardiogram functional parameters between pilots who fly HSG aircraft and pilots who fly other types of aircraft (Ref 8)" (Null hypothesis). In view of the fact that our prime concern was to refute or establish a definable structural or functional change in the heart, we decided to limit statistical echocardiographic comparisons to the measurements listed in Table II. Many of these measurements, being inter-related, would provide an internal check on the consistency of our observations. This decision was made early, before any data analysis had been undertaken.

<u>TABLE I</u>+

1. Right ventricular internal diameter - M-mode. (MM-RV)
2. Left ventricular internal diameter - M-mode. (MM-LV)
3. Inter-ventricular septal thickness in diastole - M-mode. (MM-VS)
4. Posterior wall thickness in diastole - M-mode. (MM-PW)
5. Aortic dimension - M-mode. (MM-AO)
6. Left atrial dimension - M-mode. (MM-LA)
7. Mitral valve - E/A. (MV E/A)
8. Tricuspid valve - E/A. (TV E/A)
9. Right ventricular internal diameter in diastole - 2 D. (2D-RV)
10. Left ventricular internal diameter in diastole - 2 D. (2D-LV)
11. Inter-ventricular septal thickness in diastole - 2 D. (2D-VS)
12. Posterior wall thickness in diastole - 2 D. (2D-PW)
13. Aortic dimension - 2 D. (2D-AO)
14. Left atrium - 2 D. (2D-LA)
15. Maximum RV dimension - 2 D. (RV MAX)
16. RV area. (RV-AR)

+See Annex C for methods of measurement.

Statistical methods

The core analyses consisted of both unadjusted and adjusted comparisons between the XX and ZZ pilots on the sixteen continuous measurements listed in Table I. Unpaired t-tests comparing mean values between the two groups provided the unadjusted analyses.

Comparisons which adjusted for age, body surface area, smoking history, exercise, and nation were carried out with analyses of covariance (Ref 16,17). The analysis of covariance *p*-values were further adjusted for multiple testing using re-sampling techniques (Ref 18). Both types of analyses are described in more detail below.

The model equation for each analysis of covariance is given as follows:

$$Y_{ijk} = \mu + P_i + N_j + \beta_1(A_{ijk}\text{-}A...)+\beta_2(B_{ijk}\text{-}B...)+\beta_3(S_{ijk}\text{-}S...)+\beta_4(E_{ijk}\text{-}...)+\varepsilon_{ijk},$$

where
μ = overall mean,
P_i= average effect of being an XX or ZZ pilot (i=1,2),
N_j= average effect of j'th nation (j=1,2,...10),
A_{ijk}= age of k'th subject within (i,j), (k=1,2,..n_{ij}),
n_{ij}= the number of subjects of the i'th pilot type in the j'th nation,
A...= overall mean age,
B_{ijk}= body surface area of subject,
B...= overall mean body surface area,
S_{ijk}= 1n(1+pack-years smoking) of subject,
S...= overall mean of 1n(1+pack-years of smoking),
E_{ijk}= 1n(avg weekly energy expenditure) of subject,
E...= overall mean of 1n(avg weekly energy expenditure), β_1, β_2, β_3, and β_4 are regression coefficients,

and ε_{ijk} = a random and normally distributed error term with a mean of zero and variance of σ^2.

Please note that while 11 countries participated, only 10 countries had data in their respective analyses. Thus, (J=1,2....10), rather than 11 countries.

The null hypothesis of principal interest being tested by this analysis is $H_0:P_1=P_2=0$, which says that the effect on the dependent variable Y of flying Type A (HSG) aircraft is no different from that of flying Type C.

All analyses of covariance were performed using the SAS GLM (Ref 19) procedure. The sources of variation and associated degrees of freedom are given below, where "Nr of subjects" is the total number of subjects with complete data for the dependent variable and all the source lines listed:

Source	Degrees Of Freedom
Pilot type (XX vs ZZ)	1
Nation of study	11
Age	1
Body surface area	1
ln(1+pack-years smoking)	1
ln(avg weekly energy expenditure)	1
Error	Nr of subjects minus 17

The SAS GLM procedure also produced a set of "least squares means" for the XX and ZZ pilot groups, which are equal if the null hypothesis is true. These are described as "the expected value of class means that you would expect for a balanced design involving the class variable with all covariates at their mean value" (Ref 19).

Perhaps a simpler way of thinking about them is that least squares means are conceptually similar to "age-adjusted mortality rates" as opposed to "crude mortality rates" (which would be like the unadjusted means from t-tests in this study).

The set of *p*-values adjusted for multiple-testing by bootstrap methods (Ref 19) (in addition to being adjusted for the covariates) was computed from 10,000 bootstrap samples using the SAS MULTTEST (Ref 20) procedure. The reason for computing these is to help control the Type I error rate that has been increased due to performing numerous tests of significance. Bootstrap adjustments for multiplicity take into account correlations among the variables being tested, in contrast to Bonferroni methods, which do not.

To assess whether a "dose-response" analysis might provide a more sensitive assessment of an effect due to HSG-exposure, we subdivided the XX pilot group into deciles of Type A flying hours and used SAS GLM to compute means of echo parameters adjusted for five covariates. Plots of the decile means were examined for monotonic trends. A similar analysis of YY and ZZ pilots provided a suitable comparison.

RESULTS

GENERAL

Echocardiographic studies were submitted from 13 NATO countries: Belgium, Canada, Denmark, France, Germany, Greece, Italy, Norway, Portugal, Spain, Turkey, the United Kingdom and the United States. The details of submitted studies by country are shown in Table 2. A total of 1611 studies, on 1434 different individuals, were submitted to the database, including 177 duplicate studies. Two hundred forty-three (243) of the 1434 studies were retrospective (obtained prior to protocol completion) and were not used in the analysis because of incomplete information. There were, then, 1191 prospective studies submitted. Of these 1191, 39 were student pilots or pilot training candidates with no flying hours. These studies had been submitted in anticipation of a longitundinal study. Of the remaining 1152 prospective studies submitted on trained pilots, 1054 (91.5%) were complete and used for this analysis (Figure 1). A complete study was defined by Working Group 18 as having at least one entry in the defined M-mode and in the defined 2-D criteria, as well as a flying history and a type II exercise history. M-mode only studies, without accompanying 2D images and measurements were not accepted as complete studies. The working group felt that inaccuracies would be introduced by allowing M-mode measurements that were not 2D directed. M-mode parameters analyzed included end-diastolic dimension of the right ventricle (MM-RV), left ventricle (MM-LV), interventricular septum (MM-VS), left ventricular posterior wall (MM-PW) and aorta (MM-AO) and end systolic dimension of the left atrium (MM-LA). Two-dimensional parameters included those same six dimensions (2D-RV, 2D-LV, 2D-VS, 2D-PW, 2D-AO, 2D-LA) plus right ventricular maximum diameter and area (RVMAX, RV-AR) in the four chamber view. Doppler variables examined were the E to A ratio for the mitral and tricuspid valves. Of the 1054 complete prospective studies, the distribution by pilot subtypes is: XX - 289 (27%), ZZ - 254 (24%), YY - 251 (24%), AB - 168 (16%) and NN - 92 (9%).

DEMOGRAPHIC DATA

Detailed demographic data were collected for each pilot. This information is presented in tables 2 through 18, with brief comments on each demographic parameter preceding the appropriate table or tables. Parameters presented include age, body surface area/height/weight, blood pressure, total and HDL cholesterol, sports activity, smoking history, and flying history (total and prior six months hours). Each table displays the number of individuals for whom that particular parameter was reported, the mean value, one standard deviation, and the range of values (minimum and maximum). Although the analysis of echocardiographic parameters was limited to XX and ZZ pilots, the entire pilot population of complete studies (1054) was used for the demographic data. This demographic information is presented for the entire group and, additionally, is further displayed by pilot subtype and country. These data should not be interpteted to reflect the prevalence of these demographic parameters in all aviators. This is a select study population

TABLE 2

SUBMITTED STUDIES BY COUNTRY

COUNTRY	ECHOS	IND	PRO	COMPLETE
Belgium	448	300	170	147
Canada	96	91	91	80
Denmark	39	39	39	38
France	228	213	213	189
Germany	66	66	26	0
Greece	270	267	257	245
Italy	3	3	3	3
Norway	85	85	85	74
Portugal	33	33	33	32
Spain	121	116	56	50
Turkey	87	87	87	76
U.K.	55	54	51	51
U.S.A.	80	80	80	69
TOTAL	1611	1434	1191	1054

NOTE: echos = total echos, ind = total # individual subjects, pro = prospective studies, complete = complete prospective echos

FIGURE 1

SUBMITTED ECHOCARDIOGRAPHIC STUDIES

1611 total echocardiographic studies submitted	
1434 individuals	177 duplicates
1191 prospective	243 retrospective
1152 prospective pilot studies	39 student pilot studies
1054 complete studies	98 incomplete studies

which has met specified inclusion and exclusion criteria, a population with no suspected cardiac problems or diagnoses, based upon regular periodic occupational examinations determined by each aviator's country. For example, this information does not reflect the distribution of blood pressures in all aviators because hypertension would have excluded an aviator from this study. The pilots in the data set are highly selected. The reader is advised that the cofactor/demographic data are not generalizable with respect to aircrew epidemiological data for any country or pilot subtype or for the NATO air forces at large.

Age data (in years) are displayed in Table 3. Mean age for the entire group was 31.4 years. Mean age for pilot subtypes ranged from 29.8 years (XX) to 33.5 years (AB). Mean age for countries ranged from 28.2 years (Turkey) to 34.6 years (United States).

TABLE 3

AGE (YEARS) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	29.8	4.6	22.0	47.0
ZZ	254	31.7	7.6	20.8	56.1
YY	248	31.3	5.5	23.1	54.2
AB	168	33.5	6.2	23.6	55.7
NN	92	31.9	7.5	22.4	54.3
TOTAL	1051	31.4	6.3	20.8	56.1
Belgium	147	33.4	7.0	20.9	53.9
Canada	80	32.7	6.5	22.0	51.3
Denmark	38	33.6	9.5	22.0	56.0
France	189	30.1	5.2	20.8	45.9
Greece	245	30.9	4.6	23.5	46.0
Italy	3	28.3	1.8	26.7	30.3
Norway	74	29.5	5.0	23.4	48.8
Portugal	32	31.2	5.5	21.7	41.9
Spain	50	29.9	6.7	22.0	51.1
Turkey	73	28.2	3.9	23.2	37.9
U.K.	51	34.0	9.3	20.8	56.1
U.S.A.	69	34.6	6.7	24.7	51.9
TOTAL	1051	31.4	6.3	20.8	56.1

= number of subjects, SD = one standard deviation, MIN = minimum value, and MAX = maximum value

Body surface area (M^2), height (cm) and weight (kg) are displayed in Tables 4, 5 and 6. Mean body surface area for the total group was 1.96 M^2. Pilot subtypes ranged from 1.93 M^2 (NN) to 1.97 M^2 (AB). Countries ranged from 1.89 M^2 (Portugal and Turkey) to 2.03 M^2 (Denmark). Mean height and weight for the total group was 178.5 cm and 77.6 kg. Mean values by pilot subtypes ranged from 177.5 cm (YY) and 76.1 kg (NN) to 179.4 cm (AB) and 78.4 kg (AB). Country means ranged from 173.8 cm (Portugal) and 72.9 kg (Turkey) to 182.9 cm (Denmark) and 81.1 kg (Denmark).

TABLE 4

BODY SURFACE AREA (M^2) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	1.96	0.12	1.67	2.28
ZZ	254	1.96	0.13	1.61	2.35
YY	251	1.95	0.12	1.57	2.28
AB	168	1.97	0.11	1.73	2.32
NN	92	1.93	0.13	1.62	2.34
TOTAL	1054	1.96	0.12	1.57	2.35
Belgium	147	1.96	0.11	1.68	2.32
Canada	80	1.99	0.14	1.68	2.34
Denmark	38	2.03	0.10	1.79	2.22
France	189	1.91	0.13	1.57	2.35
Greece	245	1.99	0.11	1.65	2.28
Italy	3	1.97	0.19	1.84	2.19
Norway	74	2.00	0.12	1.72	2.29
Portugal	32	1.89	0.11	1.68	2.06
Spain	50	1.93	0.11	1.67	2.20
Turkey	76	1.89	0.10	1.67	2.17
U.K.	51	1.97	0.11	1.75	2.24
U.S.A.	69	1.96	0.12	1.69	2.30
TOTAL	1054	1.96	0.12	1.57	2.35

TABLE 5

HEIGHT (CM) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	178.9	5.4	167.0	192.0
ZZ	254	178.9	6.2	160.0	193.0
YY	251	177.5	5.4	160.0	193.0
AB	168	179.4	5.1	167.0	194.0
NN	92	177.7	5.7	165.0	190.0
TOTAL	1054	178.5	5.6	160.0	194.0
Belgium	147	179.0	5.0	168.0	194.0
Canada	80	179.0	6.1	168.0	192.0
Denmark	38	182.9	4.2	172.0	188.0
France	189	177.8	6.1	160.0	191.0
Greece	245	178.4	5.0	167.0	190.0
Italy	3	177.7	8.3	171.0	187.0
Norway	74	181.9	5.1	168.0	193.0
Portugal	32	173.8	5.8	162.0	184.0
Spain	50	177.2	4.9	167.0	190.0
Turkey	76	177.0	5.0	168.0	187.0
U.K.	51	179.4	5.4	169.0	190.0
U.S.A.	69	177.8	6.1	160.0	193.0
TOTAL	1054	178.5	5.6	160.0	194.0

TABLE 6

WEIGHT (KG)
BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	77.3	8.2	58.0	106.0
ZZ	254	77.4	9.2	56.0	109.0
YY	251	78.1	8.3	50.0	102.0
AB	168	78.4	8.2	63.0	109.0
NN	92	76.1	9.1	56.0	107.0
TOTAL	1054	77.6	8.6	50.0	109.0
Belgium	147	77.6	8.6	60.0	106.0
Canada	80	80.0	10.2	59.0	107.0
Denmark	38	81.1	7.1	65.0	96.0
France	189	73.6	8.6	50.0	109.0
Greece	245	80.6	7.5	58.0	100.0
Italy	3	79.3	11.9	72.0	93.0
Norway	74	79.5	8.4	60.0	100.0
Portugal	32	74.8	7.2	62.0	88.0
Spain	50	75.5	7.3	60.0	92.0
Turkey	76	72.9	6.9	58.0	91.0
U.K.	51	78.0	7.5	65.0	97.0
U.S.A.	69	78.1	7.9	61.0	109.0
TOTAL	1054	77.6	8.6	50.0	109.0

Blood pressure (seated, mm Hg) is displayed in Tables 7 and 8. Mean sitting systolic and diastolic values for the group were 124.2/77.9 mm Hg. Pilot subtypes ranged from 122.2/77.1 mm Hg (YY/NN) to 125.4/78.4 mm Hg (ZZ/XX). Country means ranged from 114.3/73.0 mm Hg (United States/Spain) to 133.0/82.2 mmHg (Italy/Turkey).

Total cholesterol and HDL cholesterol (mmol/L) are displayed in Tables 9 and 10. Mean values for the group were 5.4/1.4 mmol/L. Pilot subtypes ranged from 5.1/1.3 mmol/L (NN/ZZ) to 5.6/1.4 mmol/L (YY/all others). Country means ranged from 4.2/1.2 mmol/L (Italy/Canada and Portugal) to 5.8/1.5 mmol/L (Turkey/France).

Type II exercise data (kj/week) from prospective subjects are displayed in Table 11. Mean for the total group was 8,250 kj/week. Pilot subtypes ranged from 5,894 kj/week (YY) to 10,224 kj/week (ZZ). Country means ranged from 3,924 kj/week (Greece) to 14,627 kj/week (Canada). The original protocol and the worksheet included a qualitative assessment of exercise (Type I history), graded by the pilot as sedentary, light, moderate or regular/heavy for both aerobic and isometric exercise. Correlation between Type I and Type II exercise histories was assessed and found to be poor. When further examined, the qualitative grading by the pilots seemed often very inaccurate when compared to the detailed exercise history given by pilots for the Type II exercise calculation. Obtaining accurate Type I qualitative grading would have required careful interview by one of the study investigators, rather than just allowing the pilot to qualitatively grade his exercise without assistance.

TABLE 7

SYSTOLIC BLOOD PRESSURE (MM HG)
BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	266	124.2	10.8	90.0	160.0
ZZ	232	125.4	13.2	90.0	180.0
YY	243	122.2	9.6	100.0	160.0
AB	148	125.3	10.5	100.0	150.0
NN	78	125.1	12.1	96.0	160.0
TOTAL	967	124.2	11.2	90.0	180.0
Belgium	79	130.6	10.6	110.0	160.0
Canada	76	128.3	14.0	100.0	180.0
Denmark	34	127.8	10.8	110.0	145.0
France	188	127.5	9.9	100.0	160.0
Greece	244	121.1	8.7	100.0	140.0
Italy	3	133.0	6.6	127.0	140.0
Norway	74	123.1	10.7	100.0	152.0
Portugal	32	124.8	9.3	100.0	148.0
Spain	48	118.9	10.8	100.0	145.0
Turkey	75	126.3	9.2	110.0	160.0
U.K.	51	124.2	13.1	100.0	158.0
U.S.A.	63	114.3	11.8	90.0	140.0
TOTAL	967	124.2	11.2	90.0	180.0

TABLE 8

DIASTOLIC BLOOD PRESSURE (MM HG)
BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	266	78.4	7.5	50.0	100.0
ZZ	232	77.2	9.6	50.0	110.0
YY	243	78.2	6.7	58.0	100.0
AB	148	77.8	8.2	60.0	106.0
NN	78	77.1	8.2	60.0	110.0
TOTAL	967	77.9	8.0	50.0	110.0
Belgium	79	79.9	9.1	60.0	110.0
Canada	76	81.8	11.1	58.0	110.0
Denmark	34	81.2	6.2	60.0	90.0
France	188	75.0	7.8	50.0	100.0
Greece	244	78.6	5.3	65.0	90.0
Italy	3	81.0	10.6	69.0	89.0
Norway	74	81.0	7.5	60.0	98.0
Portugal	32	73.7	6.4	60.0	81.0
Spain	48	73.0	7.8	58.0	90.0
Turkey	75	82.2	5.3	70.0	100.0
U.K.	51	75.1	8.8	54.0	100.0
U.S.A.	63	73.6	8.0	58.0	92.0
TOTAL	967	77.9	8.0	50.0	110.0

TABLE 9

TOTAL CHOLESTEROL (MMOL/L) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	199	5.4	0.8	3.6	7.5
ZZ	143	5.3	1.0	2.6	8.8
YY	199	5.6	0.8	3.5	8.9
AB	139	5.4	1.0	2.6	9.1
NN	68	5.1	0.8	3.5	7.1
TOTAL	748	5.4	0.9	2.6	9.1
Belgium	143	5.4	0.9	3.8	9.1
Canada	10	4.7	1.0	3.5	7.1
Denmark	0	--	--	--	--
France	167	5.1	0.9	2.6	7.5
Greece	230	5.5	0.8	3.6	8.9
Italy	1	4.2	--	4.2	4.2
Norway	0	--	--	--	--
Portugal	32	5.4	1.2	3.5	8.1
Spain	50	5.2	0.6	4.2	7.7
Turkey	76	5.8	0.7	4.2	8.0
U.K.	39	5.4	1.1	2.6	8.0
U.S.A.	0	--	--	--	--
TOTAL	748	5.4	0.9	2.6	9.1

TABLE 10

HDL CHOLESTEROL (MMOL/L) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	122	1.4	0.2	0.9	2.1
ZZ	105	1.3	0.3	0.6	2.3
YY	111	1.4	0.3	0.7	2.4
AB	111	1.4	0.3	0.5	2.3
NN	60	1.4	0.3	0.8	2.3
TOTAL	509	1.4	0.3	0.5	2.4
Belgium	141	1.3	0.3	0.5	2.4
Canada	10	1.2	0.3	0.8	1.7
Denmark	0	--	--	--	--
France	105	1.5	0.3	0.9	2.3
Greece	80	1.3	0.1	1.1	1.8
Italy	0	--	--	--	--
Norway	0	--	--	--	--
Portugal	32	1.2	0.4	0.7	2.3
Spain	50	1.4	0.2	0.8	1.8
Turkey	76	1.4	0.2	0.9	1.8
U.K.	15	1.4	0.4	0.7	2.1
U.S.A.	0	--	--	--	--
TOTAL	509	1.4	0.3	0.5	2.4

TABLE 11

TYPE II EXERCISE (KJ/WEEK) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	8,098	8,292	50	47,350
ZZ	254	10,224	10,487	50	73,730
YY	251	5,894	8,190	46	62,316
AB	168	8,523	9,276	53	55,973
NN	92	9,206	7,109	48	31,981
TOTAL	1,054	8,250	9,029	46	73,730
Belgium	147	7,326	6,664	48	36,552
Canada	80	14,627	11,130	66	41,701
Denmark	38	9,243	8,233	74	39,996
France	189	11,254	10,798	467	73,730
Greece	245	3,924	3,407	54	22,604
Italy	3	14,035	11,018	6,259	26,644
Norway	74	11,956	11,729	512	58,813
Portugal	32	6,721	11,086	48	62,316
Spain	50	4,745	4,239	51	17,967
Turkey	76	4,406	7,457	46	44,924
U.K.	51	9,671	8,464	763	57,703
U.S.A.	69	11,615	9,446	56	39,510
TOTAL	1,054	8,250	9,029	46	73,730

Smoking history (pack years) is displayed in Tables 12, 13 and 14. Mean value for smoking for the entire group was 3.3 pack years. Pilot subtypes ranged from 2.5 pack years (NN) to 4.2 pack years (YY). Country means ranged from 1.5 pack years (Norway) to 4.8 pack years (Greece). (Table 12). The smoking data in Table 12 are somewhat misleading because of inclusion of nonsmokers. In the entire group, there were 60% nonsmokers, 9% former smokers and 31% active smokers. Details by pilot subtype and country are shown in Table 13. Table 14 details the mean and maximum pack years of smoking for former and active smokers only. The total number of former and active smokers differs slightly between Tables 13 and 14; twelve subjects did not report their total pack years and are therefore excluded from Table 14.

Flying hours are displayed in Tables 15, 16, 17 and 18. Mean total hours for the entire group was 1,890. Pilot subtypes ranged from 1,347 hours (XX) to 2,512 hours (ZZ). Country means ranged from 932 hours (Italy) to 3,738 hours (United Kingdom). Table 15 details total hours for the entire group, as well as by pilot subtype and country. Table 16 shows mean total flying hours divided into mean type A, B and C flying hours. Tables 17 and 18 provide the same detailed information for flying hours, limited to the six months previous to the echocardiogram. These tables do not include the subtraction correction for training hours; thus, A + B + C hours equals total hours. Also, the mean hours in Tables 17 and 18 differ slightly because of computation and rounding differences.

TABLE 12

SMOKING HISTORY (PACK YEARS) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	286	2.6	5.0	0.0	30.0
ZZ	248	2.9	6.8	0.0	50.0
YY	246	4.2	7.6	0.0	60.0
AB	167	4.0	6.4	0.0	42.0
NN	90	2.5	5.7	0.0	31.5
TOTAL	1037	3.3	6.4	0.0	60.0
Belgium	146	3.7	6.7	0.0	31.5
Canada	77	2.6	5.8	0.0	30.0
Denmark	37	2.7	7.6	0.0	40.0
France	187	1.9	4.0	0.0	22.8
Greece	245	4.8	6.9	0.0	40.0
Italy	3	3.3	5.8	0.0	10.0
Norway	68	1.5	7.4	0.0	60.0
Portugal	29	3.9	6.7	0.0	25.5
Spain	50	2.7	6.6	0.0	42.0
Turkey	75	4.3	6.0	0.0	32.0
U.K.	51	3.0	5.8	0.0	20.0
U.S.A.	69	2.5	7.7	0.0	50.0
TOTAL	1037	3.3	6.4	0.0	60.0

TABLE 13

SMOKING CATEGORIES BY PILOT SUBTYPE AND COUNTRY

GROUP	#	NONSMOKERS #	%	FORMER #	%	ACTIVE #	%
XX	289	179	62%	18	6%	92	32%
ZZ	254	170	67%	26	10%	58	23%
YY	251	139	55%	19	8%	93	37%
AB	168	88	53%	19	11%	61	36%
NN	92	55	60%	13	14%	24	26%
TOTAL	1054	631	60%	95	9%	328	31%
Belgium	147	85	58%	21	14%	41	28%
Canada	80	55	69%	10	12%	15	19%
Denmark	38	29	76%	2	5%	7	19%
France	189	125	66%	8	4%	56	30%
Greece	245	123	50%	17	7%	105	43%
Italy	3	2	67%	0	0%	1	33%
Norway	74	55	74%	6	8%	13	18%
Portugal	32	14	44%	8	25%	10	31%
Spain	50	31	62%	3	6%	16	32%
Turkey	76	28	37%	1	1%	47	62%
U.K.	51	33	65%	8	16%	10	19%
U.S.A.	69	51	74%	11	16%	7	10%
TOTAL	1054	631	60%	95	9%	328	31%

TABLE 14

SMOKING HISTORY (PACK YEARS) FOR FORMER AND ACTIVE SMOKERS ONLY

GROUP	#	FORMER MEAN	MAX	#	ACTIVE MEAN	MAX
XX	18	6.0	19.2	90	7.1	30.0
ZZ	26	10.6	50.0	55	7.9	40.0
YY	16	11.1	36.0	92	9.2	60.0
AB	18	6.4	16.0	61	9.0	42.0
NN	12	6.9	20.0	23	6.2	31.5
TOTAL	90	8.4	50.0	321	8.2	60.0
Belgium	20	7.0	23.0	41	9.7	31.5
Canada	9	10.4	20.0	13	8.0	30.0
Denmark	1	10.0	10.0	7	12.6	40.0
France	8	6.6	10.0	54	5.6	22.8
Greece	17	12.3	36.0	105	9.3	40.0
Italy	0	--	--	1	10.0	10.0
Norway	6	2.0	3.0	12	7.4	60.0
Portugal	6	5.2	15.7	9	9.1	25.5
Spain	3	3.7	5.0	16	7.7	42.0
Turkey	1	2.5	2.5	46	7.0	32.0
U.K.	8	10.5	20.0	10	6.7	20.0
U.S.A.	11	10.0	50.0	7	9.3	27.0
TOTAL	90	8.4	50.0	321	8.2	60.0

TABLE 15

TOTAL FLYING HOURS BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	1,347	809	50	4,565
ZZ	254	2,512	2,372	30	17,600
YY	251	1,598	989	231	4,550
AB	168	2,169	1,213	140	8,960
NN	92	2,164	2,339	340	17,400
TOTAL	1,054	1,890	1,638	30	17,600
Belgium	147	2,056	1,361	310	7,790
Canada	80	2,604	2,295	145	9,525
Denmark	38	1,984	1,780	320	9,700
France	189	1,839	1,334	177	6,420
Greece	245	1,482	834	280	4,400
Italy	3	932	284	760	1,260
Norway	74	1,569	1,078	50	4,565
Portugal	32	1,695	1,069	30	3,600
Spain	50	1,761	1,586	330	8,600
Turkey	76	1,149	794	231	3,412
U.K.	51	3,738	3,599	38	17,600
U.S.A.	69	2,264	1,934	92	11,100
TOTAL	1,054	1,890	1,638	30	17,600

TABLE 16

MEAN FLYING HOURS (HRS) BY PILOT SUBTYPE AND COUNTRY

GROUP	#	HRS	A HRS	B HRS	C HRS
XX	289	1347	1029	277	41
ZZ	254	2512	14	148	2350
YY	251	1598	60	1518	20
AB	168	2169	862	1212	95
NN	92	2164	397	890	877
TOTAL	1054	1890	472	744	674
Belgium	147	2056	539	799	718
Canada	80	2604	449	896	1259
Denmark	38	1984	995	609	380
France	189	1839	708	520	611
Greece	245	1482	444	1037	1
Italy	3	932	334	290	308
Norway	74	1569	515	305	749
Portugal	32	1695	0	1248	447
Spain	50	1761	457	287	1017
Turkey	76	1149	249	846	54
U.K.	51	3738	285	397	3056
U.S.A.	69	2264	91	834	1339
TOTAL	1054	1890	472	744	674

TABLE 17

TOTAL FLYING HOURS PAST 6 MONTHS BY PILOT SUBTYPE AND COUNTRY

GROUP	#	MEAN	SD	MIN	MAX
XX	289	64	51	0.0	480
ZZ	254	120	173	0.0	1850
YY	251	52	53	0.0	250
AB	168	70	156	0.0	1993
NN	92	128	256	0.0	2000
TOTAL	1054	81	138	0.0	2000
Belgium	147	80	52	0.0	350
Canada	80	93	117	0.0	450
Denmark	38	92	78	30.0	480
France	189	94	59	0.0	350
Greece	245	45	39	0.0	145
Italy	3	81	69	12.0	150
Norway	74	110	60	0.0	220
Portugal	32	79	49	0.0	200
Spain	50	103	75	0.0	300
Turkey	76	27	229	0.0	1993
U.K.	51	138	94	0.0	500
U.S.A.	69	125	408	0.0	2000
TOTAL	1054	81	138	0.0	2000

TABLE 18

MEAN FLYING HOURS PAST 6 MONTHS BY PILOT SUBTYPE AND COUNTRY

GROUP	#	HRS	A HRS	B HRS	C HRS
XX	289	64	56	7	1
ZZ	254	121	4	8	109
YY	251	52	5	45	2
AB	168	70	50	7	13
NN	92	127	38	32	57
TOTAL	1054	80	28	18	34
Belgium	147	79	33	14	32
Canada	80	94	18	32	44
Denmark	38	92	70	8	14
France	189	95	65	9	21
Greece	245	45	13	32	0
Italy	3	81	4	27	50
Norway	74	111	41	5	65
Portugal	32	80	4	49	27
Spain	50	103	24	8	71
Turkey	76	27	1	0	26
U.K.	51	138	17	0	121
U.S.A.	69	125	4	37	84
TOTAL	1054	80	28	18	34

ECHOCARDIOGRAPHIC (ECHO) PARAMETERS

Echo parameters for XX versus ZZ pilots were compared and the results adjusted for five covariates of age, body surface area, exercise, smoking and country of origin. Echo parameters were also adjusted for comparison of multiple parameters. (Tables 19, 20 and 21). An adjustment for the comparison of multiple parameters was introduced because the large number of parameters would result in an increased likelihood of a Type I error (i.e. finding a differnce between the two groups when none actually existed). Smoking and exercise had very asymmetric distributions and wide ranges of measurements. They were therefore analyzed in natural logarithmic units to minimize any subsequent skewing effect. There was a significant difference ($p<0.001$) between the two groups for age but not for body surface area, exercise or smoking. (Table 19). The XX and ZZ mean values in Table 19 differ slightly from those show earlier in Tables 3 and 4. Thirty-four studies had to be deleted from the analysis of echocardiographic parameters and are not reflected in Tables 19-21. However, their demographic information was used in the broader presentation of demographic data in Tables 3 and 4, thus accounting for the slight difference. Table 20 displays the nonadjusted and covariate adjusted mean value of each echo parameter for both XX and ZZ pilots. Table 21 displays the adjusted mean value of each echo parameter for XX versus ZZ pilots with three different p values: nonadjusted, after adjustment for the above five covariates, and after additional adjustment for multiple parameters compared. After these

several adjustments, there was no statistically significant difference ($p<0.05$ or more significant) between XX and ZZ pilots for any of the examined echo parameters.

Even prior to any adjustments, there was no significant difference between XX and ZZ pilots for MM-RV, 2D-RV or RV-AR. Prior to adjustments, there was a statistically significant difference for RVMAX, with XX pilots having a larger RVMAX than ZZ pilots, a difference which was no longer significant after adjusting for the covariates, and which remained insignificant after further adjusting for multiple parameters. Furthermore, the mean value of each echo parameter for both XX and ZZ pilots was well within the limits of established normal findings. None of the mean echo values reported in this study represented an "abnormal" value by contemporary norms. The appendix to this report displays the data in greater detail via graphs and scattergrams, including pilot subtypes other than XX and ZZ. We further examined mean echocardiographic measurements for XX and ZZ pilots by decile of total flying hours to assure that a dose response effect of flying time on these parameters was not present. Again, no dose response effect was demonstrated, and this information is displayed graphically in the appendix.

TABLE 19

COVARIATES

COVARIATE	XX MEAN	ZZ MEAN	P-VALUE
Age	29.90	31.90	<0.001
BSA	1.96	1.95	0.470
Ln-smoking	0.68	0.66	0.810
Ln-sports	8.41	8.59	0.150

Ln-smoking and Ln-sports = natural logarithmic units of smoking and sports activity, see statistical methods section and also text above

Nonadjusted comparisons, covariate adjusted comparisons, and multiple parameters adjusted comparisons are displayed in Table 21.

Nonadjusted comparisons (Table 21): Nonadjusted comparison of XX and ZZ pilots yielded six parameters that were statistically significant ($p<0.05$ or more significant). The six parameters were MM-VS, 2D-VS, MM-PW, 2D-PW, 2D-LA and RVMAX. Three of the four measurements of left ventricular wall thickness (MM-VS, 2D-VS and MM-PW) were significantly greater in ZZ pilots. 2D-PW was significantly greater in XX pilots. However, all four mean values of wall thickness were less than 1.0 cm, within established normals. Wall thickness was primarily greater in ZZ pilots, who tended to exercise more than XX pilots, although the difference in exercise was not statistically

TABLE 20

ECHO RESULTS
NONADJUSTED AND ADJUSTED MEAN VALUES

ECHO (CM)	XX NONAD	XX ADJCV	ZZ NONAD	ZZ ADJCV
MM-RV	2.15	2.12	2.08	2.06
2D-RV	2.22	2.21	2.20	2.16
MM-LV	5.07	5.09	5.07	5.10
2D-LV	4.96	4.94	5.00	5.01
MM-VS	0.91	0.92	0.95	0.95
2D-VS	0.93	0.93	0.97	0.96
MM-PW	0.85	0.86	0.89	0.87
2D-PW	0.92	0.96	0.96	0.95
MM-AO	3.01	3.02	2.99	2.95
2D-AO	3.00	3.02	3.04	2.95
MM-LA	3.42	3.48	3.44	3.46
2D-LA	3.22	3.32	3.33	3.36
RVMAX	3.50	3.69	3.62	3.65
RV-AR	19.00	19.50	19.80	20.10
MVE/A	1.62	1.62	1.64	1.62
TVE/A	1.64	1.67	1.68	1.66

NOTE: NONAD = nonadjusted mean values; ADJCV = means after adjustment for covariates age, smoking, exercise, BSA and country of origin; MM = M-mode, 2D = two-dimensional, RV = right ventricle, LV = left ventricle, VS = interventricular septum, PW = left ventricular posterior wall, AO = aorta, LA = left atrium, RVMAX = right ventricular maximum diameter, and RV-AR = right ventricular area. All measurements end-diastole except LA which is end-systole. RVMAX and RV-AR performed in the four chamber view. MV/EA and TV/EA = mitral valve and tricuspid valve E to A ratio.

significant. There was a significant difference in 2D-LA with ZZ pilots measuring greater than XX. However, there was no significant difference in MM-LA between XX and ZZ pilots. The absolute mean values for both pilot groups were very similar and again well within established normal values. As previously noted, RVMAX was also significantly greater in XX pilots with both pilot groups' mean values well within established clinical normal ranges.

Covariate adjusted comparisons (Table 21): After adjusting for the five covariates, only two echo parameters were significantly different (MM-VS and MM-AO). MM-VS remained significantly different while 2D-VS and both measurements of posterior wall thickness (MM-PW, 2D-PW) became insignificant. MM-AO became significantly different with XX pilots being larger while 2D-AO remained insignificant. 2D-LA became insignificant while MM-LA remained insignificant. The difference for RVMAX was no longer statistically significant. Again, the absolute mean values

for these two echo parameters were very similar and well within established normal values.

Multiple parameters adjustment comparisons (Table T): After additional adjustment for examining multiple parameters, there were no statistically significant differences between XX and ZZ pilots for any of the parameters. The p-value was 0.37 for MM-AO, 0.42 for MM-VS and 0.77 for 2D-AO. All other p-values were greater than 0.90.

TABLE 21

ECHO RESULTS

ECHO (CM)	XX MEANS	ZZ MEANS	P-VAL NONAD	P-VAL ADJCV	P-VAL ADJMT
MM-RV	2.12	2.06	0.130	0.24	0.98
2D-RV	2.21	2.16	0.730	0.44	>0.99
MM-LV	5.09	5.10	0.940	0.93	>0.99
2D-LV	4.94	5.01	0.450	0.22	0.97
MM-VS	0.92	0.95	0.002	0.04	0.42
2D-VS	0.93	0.96	0.020	0.19	0.95
MM-PW	0.86	0.87	0.001	0.82	>0.99
2D-PW	0.96	0.95	0.004	0.60	>0.99
MM-AO	3.02	2.95	0.350	0.03	0.37
2D-AO	3.02	2.95	0.260	0.10	0.77
MM-LA	3.48	3.46	0.710	0.59	>0.99
2D-LA	3.32	3.36	0.010	0.44	>0.99
RVMAX	3.69	3.65	0.030	0.51	>0.99
RV-AR	19.50	20.10	0.100	0.20	0.96
MVE/A	1.62	1.62	0.640	0.86	>0.99
TVE/A	1.67	1.66	0.390	0.84	>0.99

NOTE: MEANS are covariate adjusted means from TABLE 20, NONAD = nonadjusted, ADJCV = adjusted for covariates age, smoking, exercise, BSA and country of origin, ADJMT = additional adjustment for multiple tests examined

MISCELLANEOUS ECHOCARDIOGRAPHIC FINDINGS

Miscellaneous findings are presented in tables 22, 23 and 24. These include valvular isufficiency by doppler, E to A velocity ratios for the two atrioventricular valves, and assorted other echocardiographic diagnoses. These data should not be interpreted to reflect the prevalence of these findings in all aviators. These are findings in a select population which has met the specified protocol inclusion and exclusion criteria, a population with no suspected cardiac findings based on regular periodic occupational examinations as determined by each aviator's country.

Doppler echo findings are displayed in Table 22. To simplify analysis of valvular insufficiency, readings were categorized as "yes" or "no" regarding the presence or absence of insufficiency of a degree felt to be clearly abnormal and not a possible physiologic normal variant. A "yes" response for aortic insufficiency meant mild, moderate or severe; a "no" response meant none or minimal. A "yes" response for the other three valves meant moderate or severe; a "no" response meant none, minimal or mild. Results are shown in Table 22. Four ZZ pilots had aortic insufficiency (AI) while none of the XX pilots had AI. Of those four ZZ pilots, three had mild AI and one had moderate AI. One XX pilot had moderate pulmonic insufficiency (PI), but there was no PI in the ZZ pilots. There was no moderate or severe mitral insufficiency in the XX or ZZ pilots. One ZZ pilot had moderate tricuspid insufficiency, but there was no tricuspid insufficiency in the XX pilots. There was no documentation of severe insufficiency of any of the four cardiac valves in any pilot subtype.

TABLE 22

DOPPLER VALVULAR INSUFFICIENCY

	AORTIC		MITRAL	
	XX	ZZ	XX	ZZ
No data	22	30	17	23
No	267	220	272	231
Yes	0	4	0	0
TOTAL	289	254	289	254

	PULMONARY		TRICUSPID	
	XX	ZZ	XX	ZZ
No data	21	28	19	26
No	267	226	270	227
Yes	1	0	0	1
TOTAL	289	254	289	254

Mitral and tricuspid valve velocity data are displayed in Table 23. Tables 20 and 21 show only the mean E to A ratio for XX versus ZZ pilots, a somewhat meaningless and artificial comparison. E to A ratios for the two valves were divided into three groups: ratio < 1.0, ratio between 1.0 and 2.0, and ratio > 2.0. Table 23 displays this information for XX versus ZZ pilots. There was no significant difference between the two pilot subtypes for a mitral or tricuspid valve E to A ratio < 1.0 or > 2.0.

Other echo diagnoses are displayed in Table 24. Three (1.0%) XX pilots and two (0.8%) ZZ pilots had mitral valve prolapse. No XX pilots and two (0.8%) ZZ pilots had a bicuspid aortic valve. Six (2.1%) XX pilots and two (0.8%) ZZ pilots had mitral valve leaflet thickening or redundancy without prolapse. One (0.3%) XX pilot and five (2.0%) ZZ pilots had aortic valve thickening or calcification of a trileaflet valve.

TABLE 23

E TO A VELOCITIES

MITRAL VALVE

	XX PILOTS #	XX PILOTS %	ZZ PILOTS #	ZZ PILOTS %
< 1.0	7	2.6	7	3.2
1.0-2.0	223	81.7	176	80.0
> 2.0	43	15.7	37	16.8
TOTAL	273	100.0	220	100.0

TRICUSPID VALVE

	XX PILOTS #	XX PILOTS %	ZZ PILOTS #	ZZ PILOTS %
< 1.0	9	3.5	7	3.3
1.0-2.0	204	79.7	166	78.7
> 2.0	43	16.8	38	18.0
TOTAL	256	100.0	211	100.0

TABLE 24

OTHER DIAGNOSES

	XX PILOTS #	XX PILOTS %	ZZ PILOTS #	ZZ PILOTS %
MVP	3	1.0	2	0.8
BAV	0	0.0	2	0.8
MVT/RED	6	2.1	2	0.8
AVT/CA++	1	0.3	5	2.0

NOTE: MVP = mitral valve prolapse, BAV = bicuspid aortic valve, MVT/RED = mitral valve thickening or redundancy, AVT/CA++ = aortic valve thickening or calcification

QUALITY CONTROL

The original protocol from Working Group 13 included an ongoing quality control (QC) of the echocardiographic studies. A video copy of all prospective echocardiograms was to be sent to the database manager. As echocardiograms arrived from each country, the database manager would select 5% of each country's studies for QC, assuring that each was technically a good quality study. The QC studies would be remeasured and reinterpreted at the database manager facility and also by the original interpreter from the country of origin. The QC studies would thus have 3 readings, one from the database manager and two from the country of origin. Any technical errors in performing or interpreting echocardiograms would be referred back to the country of origin for correction and the corrected data entered into the database. The three sets of measurements would allow calculation of intraobserver variability for each country and interobserver variability between the database manager and each country. Limits of acceptable variability were defined and corrective procedures were established for unacceptable variabilities.

Because of several personnel changes at the database manager facility and other technical problems, Working Group 18 was unable to follow this procedure. An alternate QC process was therefore adopted by Working Group 18. After submission of all prospective studies, a single QC interpreter (cardiologist) at the database manager facility measured and interpreted a sample of echocardiograms from each country. The larger of ten studies from each country or 5% of the total number of studies from each country was reviewed. Italy submitted only three studies and all three were reviewed. The QC interpreter at the database manager facility performed duplicate measurements on all of the QC selected studies. This allowed intraobserver variability calculation for the QC interpreter and interobserver variability calculation between the QC interpreter and each country. During this QC review, a consistent technical error in the 2D measurement of the left atrium was identified in three countries. The measurement was frequently performed at end ventricular diastole instead of end ventricular systole. The 2D dimensions for aorta and left atrium were remeasured for all studies submitted by those three countries. The corrected measurements are used in the database analysis but the original values are used for the QC interobserver variability calculations.

In the original protocol, acceptable variability was defined as less than or equal to 25% for left ventricular wall thickness (septum and posterior wall) and less than or equal to 10% for all other parameters. These guidelines may be used for comparison to the actual inter/intraobserver variability calculated under the new QC process.

DATABASE MANAGER FACILITY QC INTERPRETER

One cardiologist skilled in echocardiographic interpretation performed all QC measurements from each country's QC sample of echocardiographic studies. He performed duplicate measurements on each study to allow calculation of his own intraobserver variability. Measurements performed included 13 of the 16 parameters reported in the results section (Table 21). Right ventricular area, RV-AR, was not able to be measured due to technical problems. Doppler E to A ratios for the mitral and tricuspid valves, MVE/A and TVE/A, were not measured. These were not parameters of primary interest. Subjectively, while reviewing the QC studies, the QC interpreter observed no technical errors in measurement of MVE/A or TVE/A from any country. Results of the QC interpreter's intraobserver variability for the 13 parameters is shown in Table 25. The mean variability (coefficient of variance, CV) for each parameter is well within the acceptable limits established in the original protocol. The QC interpreter's intraobserver variability was calculated for each country's QC studies reviewed by him; the range of these variabilities is shown in Table 25 as CV RANGE. The maximum variability for each parameter is also within the acceptable limits established by the original protocol.

TABLE 25

QC INTERPRETER INTRAOBSERVER VARIABILITY

ECHO	DF	MEAN	SD	CV (%) MEAN (RANGE)
MM-RV	115	2.14	0.09	4.32 (2.63-5.40)
2D-RV	115	2.12	0.10	4.80 (2.30-6.48)
MM-LV	115	5.12	0.11	2.19 (1.45-3.14)
2D-LV	115	5.10	0.12	2.34 (0.87-3.95)
MM-VS	115	0.91	0.06	6.73 (4.28-10.0)
2D-VS	115	0.90	0.06	7.04 (5.41-9.46)
MM-PW	115	0.87	0.06	6.92 (5.39-9.01)
2D-PW	115	0.90	0.06	6.96 (4.10-9.73)
MM-AO	115	3.05	0.09	3.00 (0.00-4.23)
2D-AO	114	3.11	0.10	3.04 (1.50-3.83)
MM-LA	115	3.51	0.10	2.72 (2.13-3.36)
2D-LA	114	3.41	0.10	2.96 (1.98-4.24)
RVMAX	114	3.74	0.12	3.11 (2.21-3.71)

ECHO = measured parameter, DF = degrees of freedom, MEAN = mean parameter measurement in cm, SD = one standard deviation in cm, CV = coefficient of variance expressed as mean CV for all countries combined and range of CVs from the individual countries

QC INTERPRETER VERSUS ALL PARTICIPATING COUNTRIES

Interobserver variability between the QC interpreter and each country was calculated for each of the above 13 echocardiographic parameters. The mean of the QC interpreter's duplicate measurements was compared to the value entered

into the database from each country for the QC sample echocardiographic studies. This information is shown in Table 26. The mean variability, CV, for each parameter except 2D-LA is within the acceptable limits previously established. 2D-LA variability (11.82%) slightly exceeds the acceptable limit of 10%. Technical error in 2D-LA measurement was identified in three countries and all 2D-LA measurements from those three countries were corrected in the database by the QC interpreter. The variability calculations in Table 26 use the uncorrected values of 2D-LA; after correction, variability was less than 10%. Most maximum CV values (from CV RANGE) exceed the original acceptable limits.

TABLE 26

INTEROBSERVER VARIABILITY

ECHO	DF	MEAN	SD	CV (%) MEAN	(RANGE)
MM-RV	115	2.11	0.15	6.86	(4.09-10.62)
2D-RV	115	2.14	0.17	7.94	(0.91-14.19)
MM-LV	115	5.11	0.22	4.35	(1.93-10.14)
2D-LV	115	5.05	0.20	4.00	(1.61-7.60)
MM-VS	115	0.92	0.08	8.21	(5.08-11.84)
2D-VS	115	0.92	0.09	9.28	(3.09-13.58)
MM-PW	115	0.86	0.09	10.21	(7.23-13.47)
2D-PW	115	0.92	0.08	9.05	(5.05-13.73)
MM-AO	115	3.03	0.17	5.53	(2.16-10.49)
2D-AO	111	3.02	0.26	8.45	(3.74-19.64)
MM-LA	115	3.46	0.23	6.63	(2.14-14.84)
2D-LA	111	3.25	0.38	11.82	(3.23-23.33)
RVMAX	113	3.67	0.30	8.19	(3.10-17.57)

DUPLICATE QC MEASUREMENTS IN EACH COUNTRY

As a separate step in the new QC process, each country performed duplicate measurements on five echocardiographic studies for calculation of intraobserver variability in each country. Duplicate measurements for QC could be made on studies previously submitted to the database or from five new echocardiographic studies performed specifically for the purpose of QC. These five studies were different studies from the ones remeasured and reinterpreted by the QC interpreter as described above and in Table 25. Ideally, the same interpreter would perform both the original and duplicate measurements within each country. However, personnel changes within each country's echocardiographic laboratory might prevent this, especially if duplicate measurements were performed on older studies previously submitted. This information is shown in Table 27. Two coefficients of variance are shown, one for duplicate measurements by the same interpreter and another for duplicate measurements by two different interpreters from the same echocardiographic laboratory. The intraobserver variability was much better with the same interpreter than with two different interpreters from the same echocardiographic laboratory. However, only two countries had different interpreters perform these duplicate measurements. The duplicate measurements from these two countries were done on previously submitted studies and the original interpreter was no longer available.

TABLE 27

WITHIN COUNTRY INTRAOBSERVER VARIABILITY

	MEAN		SD		CV (%)	
ECHO	SAME	DIFF	SAME	DIFF	SAME	DIFF
MM-RV	2.06	2.21	0.16	0.29	7.90	13.19
2D-RV	2.14	2.14	0.19	0.25	8.81	11.73
MM-LV	5.18	5.26	0.18	0.34	3.54	6.53
2D-LV	5.11	5.35	0.18	0.29	3.43	5.32
MM-VS	0.90	1.02	0.09	0.14	9.70	13.86
2D-VS	0.90	0.97	0.07	0.16	7.83	16.55
MM-PW	0.85	0.96	0.08	0.22	9.74	23.30
2D-PW	0.90	1.03	0.09	0.12	9.65	11.75
MM-AO	2.98	3.10	0.10	0.12	3.26	3.89
2D-AO	2.90	3.21	0.16	0.42	5.34	13.18
MM-LA	3.50	3.68	0.13	0.29	3.66	7.86
2D-LA	3.25	3.64	0.16	0.55	4.82	15.19
RVMAX	3.70	3.45	0.14	0.55	3.85	16.01
RV-AR	18.04	18.21	1.05	3.59	5.83	19.73
MVE/A	1.77	1.78	0.20	0.22	11.32	12.10
TVE/A	1.65	1.48	0.19	0.41	11.67	27.76

SAME = duplicate measurements by same interpreter
DIFF = duplicate measurements by different interpreter

APPENDICES A-C

Appendices A-C are included to present the database results in greater detail for the interested reader. This information is not necessary for an understanding of the results of this project which are presented and discussed earlier in this publication. This information is offered to the interested reader who would like a more detailed view of the database.

Appendix A: This section presents all of the measurements of the 16 echocardiographic parameters from the entire prospective database displayed in eight scattergrams. The scattergrams provide the reader with a visual display of all the measured parameters further divided into the three pilot subtypes of XX, ZZ and all other pilot types.

Appendix B: Although analysis of the database revealed no significant difference in the measured echocardiographic parameters between XX and ZZ pilots, a dose-related effect of high performance (XX) flying might have been missed. Such an effect was considered but was found not to be present. Appendix B displays the results of this analysis in several graphs. Adjusted means for each echocardiographic parameter were calculated for each decile of flying hours in XX and ZZ pilots. These "by decile" means demonstrate no dose-related effect of XX versus ZZ flying for any of the echocardiographic parameters.

Appendix C: The demographic data and the echcocardio-graphic measurements are presented in graphs by country and by pilot type, XX versus ZZ, within each country.

DISCUSSION

The initial effect of +Gz exposure (Ref 21) is increased weight of all body tissues and fluids including blood, with accumulation of blood in the distensible areas of the lower body. This results in distension of the capacitance vessels and reduction of venous return to the right heart. These initial alterations result in an immediate and progressive fall in mean arterial pressure during the first 6-12 seconds of +Gz exposure. The fall in arterial blood pressure above the heart simulates carotid sinus and upper thoracic baroreceptors, resulting in a reflex tachycardia, increased cardiac contractility and arterial constriction, and also an increase in tone in the capacitance vessels which increases venous return. These compensatory mechanisms tend to restore the mean arterial pressure at the level of the heart. At higher levels of +Gz exposure the hemodynamic effects are more pronounced, but may be alleviated by the effect of the inflated anti-G suit which predominantly supports cardiac afterload by increasing arterial resistance but may also promote venous return. With +Gz offset, as the hydrostatic effects reverse, there is a rapid increase in venous return and transient distension of the right ventricle.

The pulmonary effects of +Gz exposure (Ref 21) result from the accentuation of ventilation-perfusion inequalities present in the normal erect lung. The upper part of the lung will be ventilated but not perfused, and the lowest part of the lung will be perfused but not ventilated. During acceleration, relative alveolar volumes decrease from top to bottom in the lung. In the basal lung zones, where the terminal airways serving the alveoli are closed, the interstitial pressure will rise, resulting in an increased vascular resistance. This series of events results in an increase in the pulmonary vascular pressure.

Concern has been expressed over the years regarding permanent changes in cardiac structure or function due to these cyclical and marked changes in pre-load and after-load. Straining maneuvers, used by fighter pilots to maintain arterial pressure during +Gz exposure, are quite similar to the effects of weight lifting, combining short duration isometric muscle work with respiratory straining. Weight lifting has actually been associated with hypertrophy of the left ventricle (Ref 22). From a theoretical point of view, repeated +Gz exposures could conceivably produce permanent changes in cardiovascular hemodynamics and cardiac chamber dimensions. Theoretical reasons exist to entertain the possibility of altered left ventricular diastolic filling pressures with resultant left atrial dilatation and/or mitral regurgitation.

The preliminary echocardiographic study by Ille, et al (Ref 6) involved 32 Mirage pilots and 34 transport pilots. The mean size of the right ventricle was within the normal values for both groups, but right ventricular dimensions were, on the average, larger among the Mirage pilots than among the transport pilots. There was also a statistically significant increase in the left atrial size and left ventricular septal thickness for the fighter pilots. Thus, the theoretical considerations of the additive effects of repeated +Gz exposure during a flying career are consistent with the preliminary findings of Ille, et al. However, a separate preliminary study by Vandenbosch, et al (Ref 7), from the Belgian Air Force, found no difference in the echo studies of fighter and transport pilots, especially with regard to right ventricular internal dimensions and left atrial dimensions. The current NATO study, likewise, revealed no significant differences in any of the selected echocardiographic parameters between the two groups of high performance pilots and transport pilots. The resultant data confirm the null hypothesis of the NATO group that there is no difference in cardiac chamber dimensions, wall thickness, or echocardiographic functional parameters between high sustained G pilots and the control group of pilots. The NATO study does not confirm the preliminary finding of Ille, et al. The much larger sample size of the NATO study, as well as controlling for multiple comparisons and confounding variables such as smoking and exercise, may explain the differences between the two studies. Further, the NATO study utilized both M-mode and 2-dimensional techniques, Doppler investigation, as well as a rough estimate of diastolic function expressed as the E to A ratio of the mitral valve velocities. The two studies were quite comparable regarding body surface area and mean flight hours.

The Aerospace Medical Community owes a debt of gratitude to the French researchers who made a preliminary study of the problem in fighter pilots (Ref 6). From the outset, the French investigators were forthright about several problems which they identified early in the dialogue regarding possible right ventricular enlargement in fighter pilots:

1) The Mirage data were preliminary and the sample size was small.
2) It is not always possible to predict in advance all of the variables which may later appear to be important.
3) A large multi-national study proposed by the French researchers seemed to be the only way to actually address this issue in a statistically valid fashion.

Impact, Strengths, and Weaknesses of the NATO Study

The NATO study is very reassuring in terms of a deleterious effect of repetitive +Gz acceleration on the echo/Doppler functions which can be obtained by contemporary technology. The strength of the study derives from the large sample size, stringent subject inclusion/exclusion criteria, and quality control of the echo studies. Rigorous statistical safeguards against finding a difference due to chance were also employed, thereby minimizing the inherent difficulty in studies with multiple internal comparisons.

Regarding limitations of the study, it is always possible that the current technology and sample size were unable to detect small differences of some parameters which actually existed. However, it must be noted that all of the parameters were well within the established limits of normal, even values for the right ventricular internal dimension, the most demanding measurement to obtain. Small trends within the ranges of normal, for any given echo variable, may have been present, but are currently undetectable by current technology and a practical sample size. Further, not all of the many echo and Doppler parameters available were compared. A comparison of every single available echo/Doppler variable would have required a sample size which was simply unobtainable. The variables chosen were those which seemed to be most likely affected by the physiology of +Gz acceleration.

Having discussed several reasons which might have produced a falsely negative result in this study, perhaps one should also contemplate the reason for the lack of a cardiac effect if, as we conclude, none exists. Perhaps there is a dose response effect of +Gz acceleration, which the fighter pilots in this study simply have not reached, since many missions in type A or type B aircraft involve little sustained +Gz acceleration. Perhaps the relatively short time spent at high +Gz by the NATO fighter pilots, even over an entire career, is insufficient to produce detectable changes. We consider this possibility somewhat unlikely, since the echo trends did not tend to show progressive gradients in a population of fighter pilots across a broad range of accumulated +Gz exposure.

The null hypothesis supported by this study applies only for contemporary high performance aircraft systems, current G profiles, and current anti-G protective equipment. As aircraft systems evolve, gravitational profiles, different both in magnitude and type, will emerge. Likewise, protective equipment will evolve further to protect the aircrew. Positive pressure breathing systems and wide-body coverage anti-gravity suits were not in use during the course of this study. While the basic issue regarding cardiac effects of +Gz acceleration has been answered for the current constellation of aircrew, aircraft, and protective equipment, the issue will need to be addressed again in the future when the mosaic is different.

A longitudinal study, spanning several decades, was one possible outcome of the current cross-sectional study. Such a longitudinal study would entail long-term followup of individual fighter and tanker bomber transport pilots, monitoring cardiovascular noninvasives from pilot training to career conclusion. Such a study would also undoubtedly entail inserting new technology into the study as new techniques evolved in cardiovascular medicine. The negative results of the cross-sectional study do not absolutely speak against a longitudinal study, but given the lack of inferential data in the cross-sectional study, a longitudinal study is considerably more questionable, especially in terms of time, funds, and effort.

Other Impact of the NATO Study

This NATO echocardiographic project was AGARD's first large, full-scale, multi-national medical epidemiological study. Aside from the importance of reaching a sustainable conclusion on a major aeromedical issue, the most important outcome of this study was that it could actually be accomplished. The echo study demonstrated convincingly that AGARD (NATO) can directly sponsor cooperative, multi-national projects, thereby addressing aeromedical issues which could not be solved by any single country. NATO affords the sample size from which aircrew epidemiological studies, with both cofactor and endpoint data, can be constituted. In addition to answering the relevant aeromedical questions,

normative aircrew data, habit patterns, risk factor tendencies, and similar data emerge. Such ancillary information would be invaluable in the areas of aircrew management, physical standards, health maintenance, and preventive programs. As a result of this NATO study, a large data base of echocardiographic studies on NATO pilots has been created, with an age range from 18-55 years. Admittedly, the data base is limited only to male pilots, but even so, the large sample size is unique when compared to other reference data for echocardiographic norms. Further, the NATO echocardiographic data base consists only of absolutely healthy individuals, initially selected for good health, and maintained in good health. When published, these norms will represent the largest published compendium of such normal data in the world. The published norms will not only be of great value in the examination of military pilots, but will also have great value in the general clinical community.

Lessons Learned from NATO's First Multi-National Medical Project

In the conduct of AGARD's first multi-national project, utilizing data gathered according to an agreed upon protocol, the learning curve was steep. The members of Working Groups 13 and 18 have made multiple observations which may be of benefit to NATO scientists who design and execute such studies in the future. The salient lessons learned are outlined here for the benefit of other NATO scientists.

Organizational Lessons

1. Four meetings over 2 years is adequate to draft and report on a protocol to AGARD. However, membership changes, due to the unpredictable nature of military assignments, often necessitates more organizational time. Member nations should make every effort to continue the participation of an original WG member, even after transfer to a new duty.

2. Assigning members of the WG to various tasks for the completion of discrete functions was very effective. However, some functions must be geographically colocated. Computer programming, quality control, and the data base should be managed within the same facility.

3. Management of a central data facility, which includes the tasks in No. 2 above, is very labor intensive for the nation which hosts the facility. The principal investigator from the NATO member country hosting the data center has great demands made on their time. The services of a data manager, quality control person, and correspondent with the field are all required. In addition to statistical services, all of the above day-to-day services become the responsibility of the nation hosting the data facility. The local central data facility manager, statistician and principle investigator must attend the WG meetings. This places a burden on the member nation, but the presence of these key personnel at WG meetings must be funded.

4. A multinational study is labor intensive, above and beyond usual WG participation, for the nation hosting the data center. Strong consideration should be given to exploring the use of contract funds to assist the data center member.

5. When a multi-national scientific project is viewed as the likely outcome of a working group, AGARD should be aware in advance that a follow on WG will be required to execute the study designed by the initial WG.

6. WG meetings should be scheduled when possible to precede other AGARD functions (panel symposium) or the Aerospace Medical Association meeting. Such dual scheduling reduces travel costs.

Scientific Lessons

1. WG's addressing "G" related issues will find that quantification of the amount and type of exposure is far more complex than the issue may appear. In the NATO Air Forces, identifying discrete examples of pure HSG pilots and pure non-HSG pilots is very difficult. When identified, the number of such "pure" subjects is quite small. It is recommended that future multi-national investigators avoid the "matched pair" protocol, since this methodology requires an impractically large screening population.

2. In order to obtain the requisite sample sizes, investigators are encouraged to categorize pilots and aircrew, with respect to "G", as they have been categorized by WG 13 and 18. Perhaps this categorization could become a NATO convention, referred to as the "AGARD Pilots/Aircraft Categories".

3. Many scientific issues, both practical and theoretical, cannot be anticipated in advance of actual protocol execution. The most relevant and serious problems with the scientific study often do not become fully apparent until data are collected and forwarded. Investigators are urged to conduct a full scale preliminary study - a "training set" - before actually entering subjects and data into the central data base. Problems of subject classification, quality control, data entry, and feedback will be identified quickly. A WG meeting to finalize the gathering of experimental data, quality control methods, and data entry should be executed by using a "training set" before any study is actually entered into the actual permanent data set. Much time and effort will be expended in retrenchment without a "training set".

4. While a multi-national study is a difficult task, the completion of such a highly structured task assures high quality data, which is generalizable to NATO members. It is recommended that NATO and AGARD continue to use the working group format for identification of aircrew problems, and to sponsor multi-national studies, using real aircrew data, when the problem seems amenable to a collaborative approach.

5. Participating member nations may wish to look at their national data as a subset of the WG data base, either for comparison or correlative studies. Member nations may also wish to use their national data as part of other internal analyses. It is recommended that subsequent AGARD WG's utilize the alpha-numeric identifier derived by WG's 13 and 18. This identifier allows national identification, can be expanded for additional identifiers, and protects the privacy of the subjects, who are not uniquely identifiable.

Other General Observations and Recommendations

1. The WG based multi-national study, under AGARD sponsorship, has produced data and observations which were unobtainable otherwise. It is recommended that AGARD study a contemporary list of significant aircrew issues in order to identify those projects which are unlikely to be undertaken without AGARD multi-national sponsorship, and are suitable for a collaborative approach.

2. It is recommended that the AMP brief AGARD on the successful completion of a collaborative project, which serves as the template for multi-national projects. The greatest lesson learned in this data-centered multi-national approach is that it can be done.

3. Once approved by the AMP, the portions of the WG 13, 18 report which are of broad general interest, especially scientific lessons learned, should be briefed to the attendees at an appropriate panel symposium.

4. AGARD could approve presentation of the scientific data and conclusions at the Scientific Meeting of the Aerospace Medical Association.

5. AGARD could approve a panel at the ASMA meeting to present the broader aspects of the echo work and its implications.

6. AGARD could approve liberal republication of the scientific report in journals relevant to the subjects.

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ANNEXES:

A. Reference 8 pp 27-28.
B. Reference 8 pp 29-31.
C. Reference 8 pp 37-51.
D. Reference 8 p 26.

ANNEXES

ANNEX A - AGARD Echocardiographic Work Sheet, Demographic Data and Flight Hours (Ref 8 - pp 27-28).

ANNEX B - AGARD Echocardiographic Work Sheet, Echo and Doppler Data (Ref 8 - pp 29-31).

ANNEX C - AGARD Echocardiographic Technical Manual (Ref 8 - pp 37-51).

ANNEX D - List of NATO Aircraft (Ref 8 - p 26).

ANNEX A

AGARD ECHOCARDIOGRAPHY WORK SHEET

All data must be entered **as of the date of the echo**

1. SUBJECT FOR

Answer yes (y) or no (n)

Cross-sectional study	☐
Longitudinal study	☐
Retrospective study	☐
For the latest is the 2-D echo available	☐
is the M-Mode available	☐

2. REASON FOR STUDY
(check one)

i. Specifically for AGARD study	☐
ii. Selection for flying training	☐
iii. Routine surveillance/experienced aircrew	☐
iv. Non cardiovascular aeromedical evaluation	☐
v. Duplicate study for variation data base	☐
vi. Repeat because echo of original study is unacceptable	☐

3. EXCLUSION CRITERIA Answer all the questions by yes (y) or no (n)

FOR BOTH CROSS-SECTIONAL AND LONGITUDINAL STUDIES :

3.1 Is the subject a pilot or pilot candidat ?	☐
3.2 Is the subject on cardiovascular drugs,other than lipid-lower age.?	☐
3.3 Is the subject free from clinically diagnosed pulmonary disease ?	☐
3.4 Is the subject male ?	☐
3.5 Is the echo of acceptable quality ?	☐
3.6 Is the subject over 17 or less than 56 years of age ?	☐
3.7 Was the echo done because of suspected cardiac disease ?	☐
3.8 Are the total flying hours and hours in the past 6 months known ?	☐

FOR CROSS-SECTIONAL STUDY

3.9 Does the pilot have a mixed fighter/transport flying history ?	☐
3.10 Is the pilot currently eligible for flying duties ?	☐
3.11 Are the essential echo parameters available ?	☐
3.12 Is the type I exercise history available ?	☐
3.13 Has the subject flown at all during the past 36 months ?	☐

FOR LONGITUDINAL STUDY

3.14 If initial echo, has the subject received his pilot wings ?	☐
3.15 Is a type II exercise history available ?	☐
3.16 Does the echo data include M-mode,2D,Color flow and Doppler ?	☐

4.IDENTIFICATION NUMBER __ __/__ __ __ /__ __ __ __ __
country code / alphanumeric / 5 digit identifier

COUNTRY CODES :

01 Belgium	02 Canada	03 Denmark	04 France	05 FRG	16 Other
06 Greece	07 Italy	08 Netherland	09 Norway	10 Portugal	
11 Spain	12 Turkey	13 UK	14 USA	15 Sweden	

5. COUNTRY IN WHICH STUDY WAS DONE __ (use 2 digit code from #4)

6. NATIONALITY OF PILOT __ (use 2 digit code from #4)

7. DATE OF BIRTH __ __/__ __/__ __ (Month/Day/Year)

IDENTIFICATION NUMBER : ___/___ ___/______

8. TYPE OF PILOT 00 Unknown 01 Fighter 02 Bomber 03 Transport 03 Rotary wing 04 Other 05 Non pilot personal

9. MILITARY FLYING HISTORY List in chronologic order each aircraft in wich the subject has a minimum of 50 hours. Begin with the first military aircraft flown Use the appendix list of aircraft types for codes.

DATE (YEAR)		AIRCRAFT TYPE		FLIGHT
BEGIN	END	NAME	CODE	HOURS

10. TOTAL FLIGHT HOURS ____

11. FLIGHT HOURS ON HSG AIRCRAFT ____

% Air combat ____
% Air intercept ____
% Air to ground ____

12. FLYING HOURS IN SIX MONTHS PRIOR TO THIS ECHO ____

% Air combat ____
% Air intercept ____
% Air to ground ____

13. DATE OF LAST FLIGHT ___/___ (Month/Year) (if #12 = 0)

14. SMOKING HISTORY Have you ever smoke ? Yes ☐ No ☐

TYPE	#PACKS/DAY	#YEARS
Cigarettes		
Cigarillos		
Cigars		
Pipe		

If ex-smoker, number of years since quitting : __ __

15. EXERCISE HISTORY (See Procedures Manual for Examples)

For TYPE I EXERCISE; fill the following box :

TYPE I	AEROBIC	ANAEROBIC
None or very little		
Light		
Moderate		
Regular/Heavy		

For TYPE II EXERCISE; fill the exercise worksheet to evaluate Kj/week over the past six months. REQUIRED for both longitudinal &cross-sectional.

Identification number : ________________

Country code : ____

Birth date : ___/___/_____

ACTIVITY	#Hours per Day	#Days per week	#Weeks past last 6 months
Aerobics			
Archery			
Badminton			
Basketball			
Bowling			
Boxing : in ring			
Boxing : sparring			
Canoeing : competition			
Canoeing : leisure			
Circuit-training			
Climbing hills : with 20 kg			
Climbing hills : with 10 Kg			
Climbing hills : with 5 Kg			
Climbing hills : with no load			
Cricket : batting			
Cricket : bowling			
Croquet			
Cycling : competition			
Cycling : leisure 15 km:h			
Cycling : leisure 8 km/h			
Field hockey			
American football			
Golf			
Gymnastic			
Horse : race, gallop			
Horse : training			
Horse : Walk			
Horse : Trot			
Ice hockey			
Judo			
Marching, rapid			
Musculation : Circuit (Men)			
Musculation : Circuit (Women)			

TYPE II EXERCISE QUESTIONNAIRE PART II

Identification number : ________________
Country code : ____
Birth date : ___/___/_____

ACTIVITY	#Hours per Day	#Days per week	#Weeks past last 6 months
Running, cross country			
Running, on the level, 5'30 per mile			
Running, on the level, 6' per mile			
Running, on the level, 7' per mile			
Running, on the level, 8' per mile			
Running, on the level, 9' per mile			
Running, on the level, 11'30 per mile			
Scuba diving, moderately active			
Scuba diving, very active			
Skiing, hard snow, on hill, maximum speed			
Skiing, hard snow, on the flat, walking			
Skiing, on the flat, moderate speed			
Skiing, powdered snow, leisure (Men)			
Skiing, powdered snow, leisure (Women)			
Snow shoeing, powdered snow			
Soccer, European football			
Squash			
Swimming : Breast stroke			
Swimming : Crawl, leisure			
Swimming : Crawl, fast			
Swimming : Backstroke			
Swimming : Sidestroke			
Swimming : Treading, normal			
Swimming : Treading, fast			
Table tennis			
Tennis			
Volleyball			
Walking : Plowed field			
Walking : Fields & hillsides			
Walking : Asphalt road			
Walking : Grass track			
Weight training			

ANNEX B

IDENTIFICATION NUMBER : __ __/__ __ __ /__ __ __ __ __

16. HEIGHT ______ (cm) **17. WEIGHT** ____ (Kg)

18. BLOOD PRESURE (mm Hg)

	Seated	Supine
systolic		
diastolic		

19.CHOLESTEROL (mg/dl) TOTAL ____ HDL ____

20. DATE OF ECHOCARDIOGRAM __ __/__ __/__ __ (Month/Day/Year)

M-MODE MEASUREMENTS :

2D Directed, short axis, below mitral valve, above papillary muscles

21	Right ventricular internal dimension/diastole	(cm)	
22	Left ventricular internal dimension/diastole	(cm)	
23	Left ventricular internal dimension/systole	(cm)	
24	Septal thickness/diastole	(cm)	
25	Septal thickness/systole	(cm)	
26	Posterior wall thickness/diastole	(cm)	
27	Posterior wall thickness/systole	(cm)	
28	Aortic dimension	(cm)	
29	Left atrial dimension	(cm)	
30	Left ventricular pre-ejection time	(millisecs)	
31	Left ventricular ejection time	(millisecs)	
32	Mitral E-F slope	(mm/sec)	
33	Heart rate	(bpm)	

BIDIMENSIONAL MEASUREMENTS

Long Axis Parasternal

34	Aortic dimension	(cm)	
35	Left atrial dimension	(cm)	

Short axis, below mitral valve, above papillary muscles.

36	Right ventricular internal dimension/diastole	(cm)	
37	Left ventricular internal dimension/diastole	(cm)	
38	Left ventricular internal dimension/systole	(cm)	
39	Septal thickness/diastole	(cm)	
40	Septal thickness/systole	(cm)	
41	Posterior wall thickness/diastole	(cm)	
42	Posterior wall thickness/systole	(cm)	

Apical Four Chamber View

43	Maximum right ventricular inter. dim./diastole	(cm)	
44	Right ventricular area/diastole	(cm)	

IDENTIFICATION NUMBER : __ __/__ __ __ /__ __ __ __ __

DOPPLER MEASUREMENTS

	AORTIC FLOW	
45	Peak velocity (m/sec)	
46	LV pre-ejec. time (msec)	
47	LV ejection time (msec)	
48	Acceleration time (msec)	
49	Insufficiency (one option)	

None	Minimal	Mild
Moderate	Severe	

	PULMONARY FLOW	
50	Peak velocity (m/sec)	
51	RV pre-ejec. time (msec)	
52	RV ejection time (msec)	
53	Acceleration time (msec)	
54	Insufficiency (one option)	

None	Minimal	Mild
Moderate	Severe	

	MITRAL VALVE	
55	Peak velocity E (m/sec)	
56	Peak velocity A (m/sec)	
57	Mitral regurgitation (one option)	

None	Minimal(just det.)	Mild(<20%)
Moderate (20-40%)	Severe (>40%)	

	TRICUSPIDE VALVE	
58	Peak velocity E (m/sec)	
59	Peak velocity A (m/sec)	
60	Tricuspid regurgitation (one opt)	

None	Minimal(just det.)	Mild(<20%)
Moderate (20-40%)	Severe (>40%)	

QUALITATIVE ECHOCARDIOGRAPHIC ASSESSMENT

61 - Are there any other echocardiographic findings ? Yes ☐ No ☐

If yes, check all positive findings.

VALVULAR

MITRAL VALVE

		AL		PL
Stenotic	62	Yes No		
Thickened	63	Yes No	68	Yes No
Redundant	64	Yes No	69	Yes No
Prolapse	65	Yes No	70	Yes No
Flail	66	Yes No	71	Yes No
Fluttering	67	Yes No	72	Yes No

AL = Anterior Leaflet
PL = Posterior Leaflet

TRICUSPID VALVE

Stenotic	73	Yes No
Thickened	74	Yes No
Redundant	75	Yes No
Prolapse	76	Yes No
Flail	77	Yes No

PULMONARY VALVE

Bicuspid	78	Yes No

AORTIC VALVE

Bicuspid	79	Yes No
Thickened	80	Yes No
Stenotic	81	Yes No
Calcified	82	Yes No

IDENTIFICATION NUMBER : __ __/__ __ __/__ __ __ __ __ __

WALLS

83	Motion abnormality	Yes No
84	Assimetric septal hypertrophy (Septal/posterior wall ratio>1.3)	Yes No

SEGMENTS (If #83 = YES)

83.1 - Anterior	Normal Hypokinetic	Dyskinetic Akinetic
83.2 - Lateral	Normal Hypokinetic	Dyskinetic Akinetic
83.3 - Posterior	Normal Hypokinetic	Dyskinetic Akinetic
83.4 - Median	Normal Hypokinetic	Dyskinetic Akinetic
83.5 - Anterior	Normal Hypokinetic	Dyskinetic Akinetic
83.6 - Lateral	Normal Hypokinetic	Dyskinetic Akinetic
83.7 - Posterior	Normal Hypokinetic	Dyskinetic Akinetic
83.8 - Median	Normal Hypokinetic	Dyskinetic Akinetic
83.9 - Apex	Normal Hypokinetic	Dyskinetic Akinetic

OTHER

Myxoma	85	Yes	No
Focal hypertropy	86	Yes	No
Septal paradox	87	Yes	No
ASD	88	Yes	No
VSD	89	Yes	No
Thrombus	90	Yes	No

91. Others (5 letters) :

ANNEX C

TECHNICAL SECTION

INTRODUCTION

Echocardiography is a contemporary method of cardiac investigation; the relative simplicity of the technique must not obscure the fact that echocardiography, whatever the equipment or the circumstances, remains crucially dependent upon the experience and expertise of the operator. The following technical recommendations are designed to minimize between-centre variability; the measurement protocols are mostly those of the American Society of Echocardiography (ASE). Additional standards have been devised by AMP WG 13 to meet the specific requirements of the proposed study. Illustrations are labeled by number and by corresponding worksheet (WS) number. This AGARD/AMP Technical Section was designed to be used in conjunction with, and referenced with, the AGARD/AMP Echocardiographic Worksheet.

PATIENT POSITION

Recumbent, full length with head slightly raised. The arterial blood pressure used for wall stress calculation will be obtained with the patient recumbent and relaxed.

EQUIPMENT SETTINGS

Minimum gain consistent with visualizing all structures to be studied, without excessive brightness. Depth compensation of gain: adjusted so that both near and distant structures are visible and the endocardial boundaries are clear. Special attention will be given to the anterior wall of the right ventricle to avoid "echo saturation" at this level and to define boundaries clearly. (This is one of the essential conditions for obtaining true measurements of the right ventricle.) Cardiac image should be sufficiently enlarged to take up essentially the whole screen; though a small picture may make measurements between surfaces seem easier, in fact, the loss of (finer) structures increases measurement errors.

STANDARD PROTOCOL FOR THE ECHO EXAMINATION

Since extra videotape will be required for quality control, please record extra footage prior to freeze-frame analysis, caliper position and measurement projection. M-mode recording and/or hard copies are required.

For the longitudinal study, the heart must be examined in all standard projections to detect any cardiac disorder that would be a bar to inclusion in the study.

M-MODE MEASUREMENTS

The necessary M-mode measurements are made using standard echo windows. For the cross-sectional prospective data as well as the longitudinal study, two-dimensional guided M-modes should be performed, such that the M-mode image is obtained while scanning in the parasternal short-axis view.

- Right Ventricular Internal Dimension Diastole (Fig. 1, WS #21)

This measurement is made by the parasternal short-axis window, below the mitral valve, at the apices of the left ventricular papillary muscles. End-diastole is marked by the onset of the ECG Q wave. The right ventricular dimension in end-diastole is measured from the posterior margin of the right ventricular anterior wall to the superi margin of the interventricular septum.

Figure 1, WS #21

- Left Ventricular Internal Dimension Diastole/Systole (Fig. 2, WS #22, #23)

These measurements are made by the parasternal short-axis window, below the mitral valve, at the apices of the left ventricular papillary muscles. Systole is defined by the maximum thickening of the left ventricular posterior wall. End-diastole is marked by the onset of the ECG Q wave.

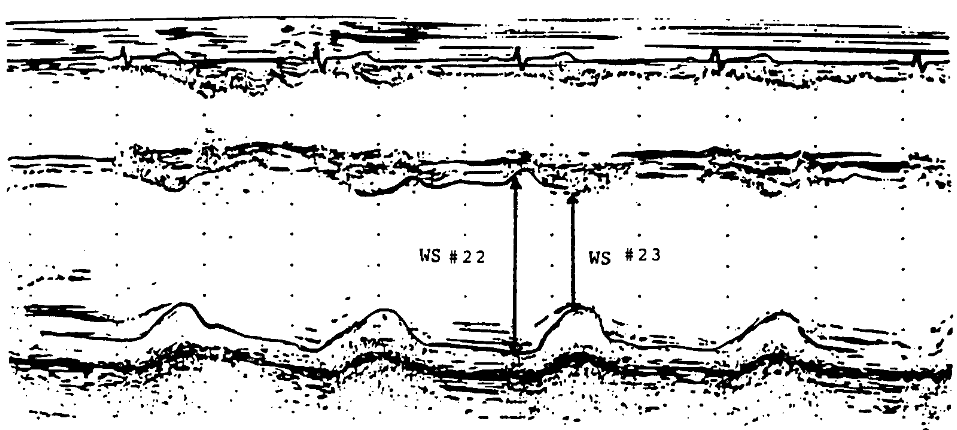


Figure 2, WS #22, #23

- Septal Thickness Diastole/Systole, Posterior Wall Thickness Diastole/Systole (Fig. 3, WS #24, #25, #26, #27)

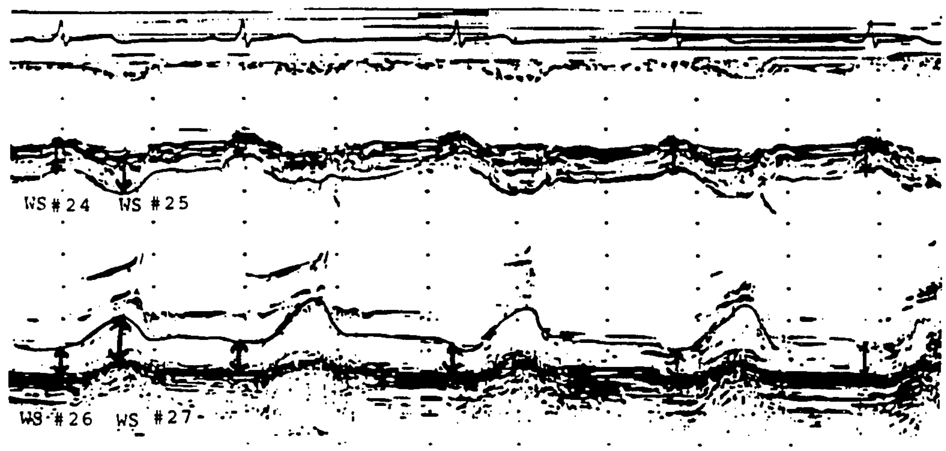


Figure 3, WS #24, #25, #26, #27

- Aortic Dimensions (Fig. 4, WS #28)

Aortic dimensions are measured at the onset of the ECG Q wave. Measurements are taken from the superior aspect of the aortic anterior wall to the superior surface of the aortic posterior wall (i.e., leading edge to leading edge).

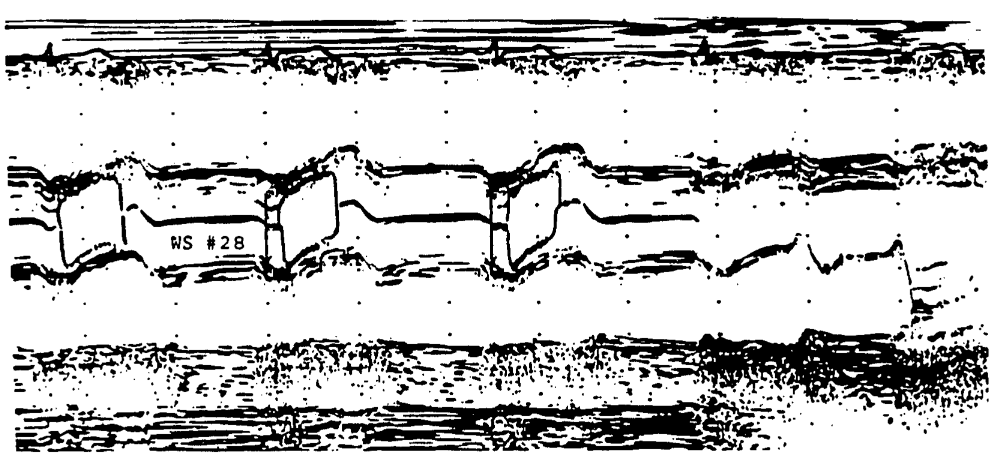


Figure 4, WS #28

- Left Atrial Dimension (Fig. 5, WS #29)

Left atrial dimensions are measured at the widest dimension at the end of ventricular systole. Measurements are obtained from the superior surface of the aortic posterior wall to the superior surface of the posterior wall of the left atrium. The measurement level corresponds with the closure point of the aortic cusps on the M-mode tracing. Special attention should be given to not including a pulmonary vein or descending aorta in the left atrial measurement.

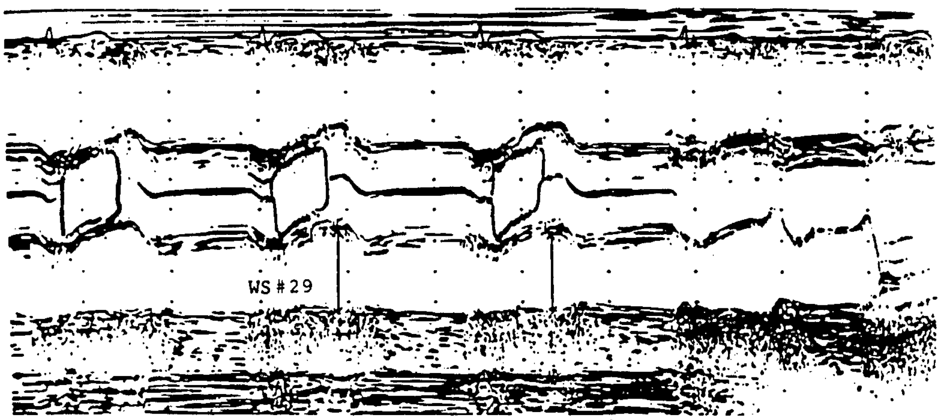


Figure 5, WS #29

- M-mode Systolic Time Intervals (Fig. 6, WS #30, #31)

These intervals require a clearly defined Q wave.

Pre-ejection period: The left ventricular pre-ejection period starts at the onset of the ECG Q wave and ends at the onset of the aortic valve opening.

Ejection period: The left ventricular ejection period starts at the onset of the aortic valve opening (opening box) and ends at valve closure.

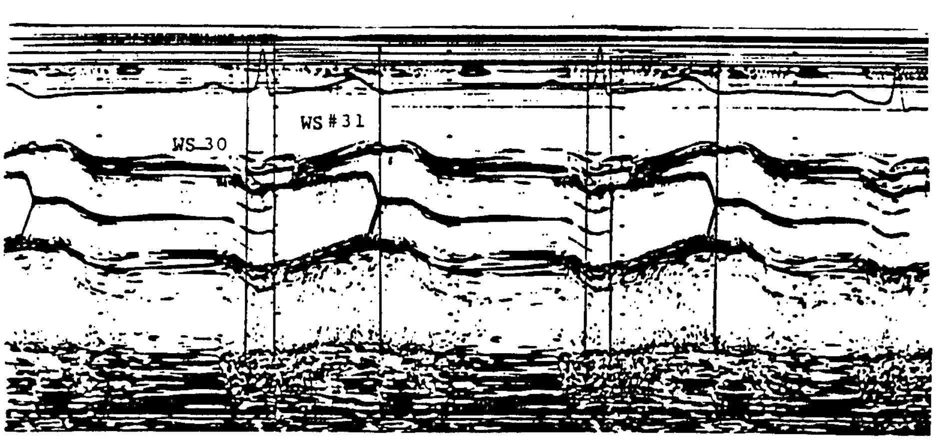


Figure 6, WS #30, #31

- E-F Slope - Mitral Valve (Fig. 7, WS #32)

Please note, attention needs to be taken that the F point be defined as the lowest point on the slope.

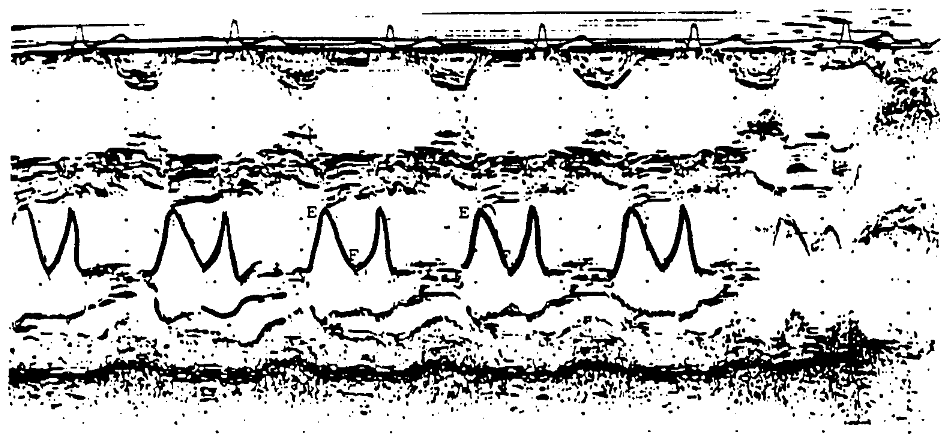


Figure 7, WS #32

TWO-DIMENSIONAL (BIDIRECTIONAL) MEASUREMENTS

In order to obtain appropriate, proper measurements, the following two-dimensional (2-D) views must be performed.

- Parasternal Long-Axis View
- Parasternal Short-Axis View, 3 levels (Fig. 8): At the base where the aortic root and aortic valve can be visualized, at the level of the mitral valve, and within the left ventricular chamber at the apices of the papillary muscles.
- Apical 4-Chamber View
- Apical 2-Chamber View

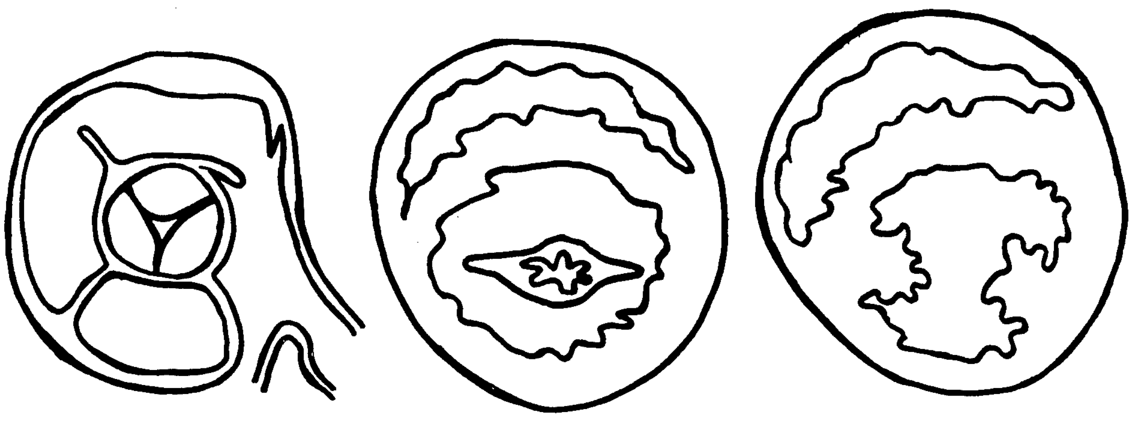


Figure 8

PARASTERNAL LONG-AXIS VIEW

- Aortic Dimension (Fig. 9, WS #34)

The aorta is measured in the anteroposterior diameter at the level of the sinuses of Valsalva. This measurement is taken at end-diastole, onset of the ECG Q wave.

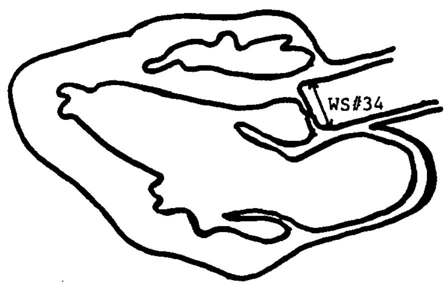


Figure 9, WS #34

- Left Atrial Dimension (Fig. 10, WS #35)

Anteroposterior dimension of the chamber from the superior surface of the aortic posterior wall to the superior surface of the left atrium. This measurement is taken at the end of ventricular systole.

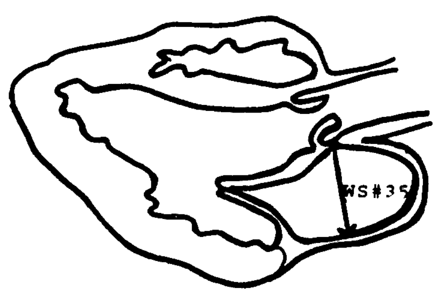


Figure 10, WS #35

PARASTERNAL SHORT-AXIS VIEW (Below the mitral valve, above or at the apices of the papillary muscles)

- Right Ventricular Internal Dimension Diastole (Fig. 11, WS #36)

Right ventricular dimension is measured from the posterior margin of the right ventricular anterior free wall to the superior margin of the intraventricular septum. End-diastole is defined as the beginning of the QRS complex.

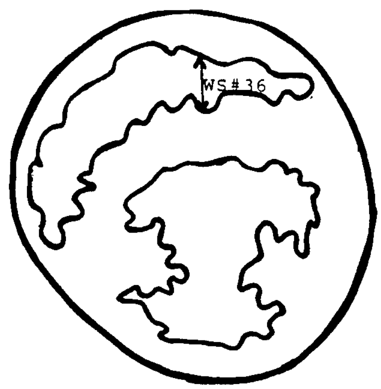


Figure 11, WS #36

- Left Ventricular Internal Dimension Diastole/Systole (Fig. 12, WS #37, #38)

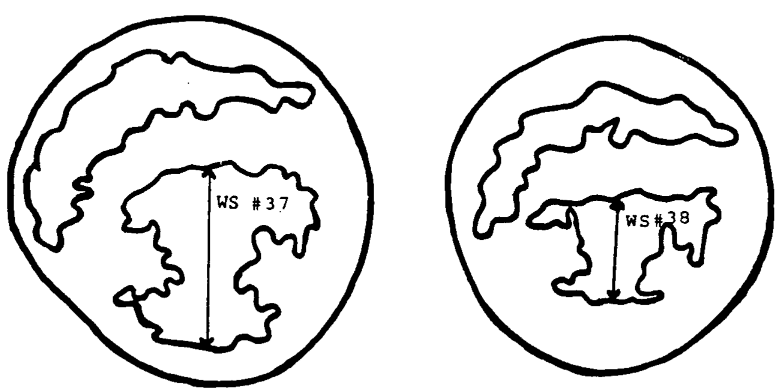


Figure 12, WS #37, #38

- Septal Thickness Diastole/Systole, Posterior Wall Thickness Diastole/Systole (Fig. 13, WS #39, #40, #41, #42)

APICAL 4-CHAMBER VIEW

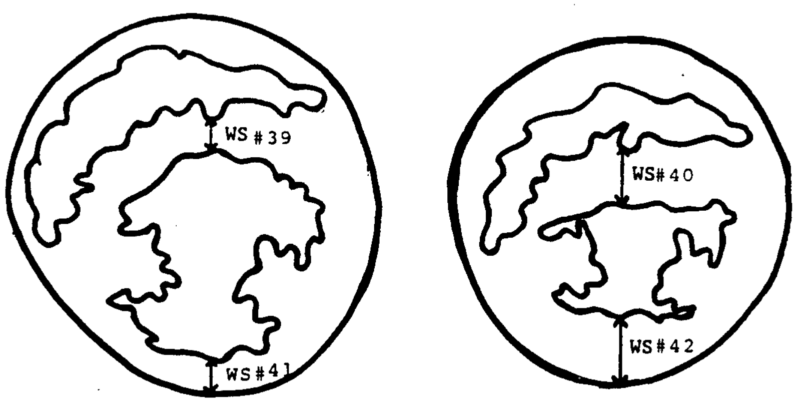


Figure 13, WS #39, #40, #41, #42

- Maximal Right Ventricular Internal Dimensions Diastole (Fig. 14, WS #43)

This measurement is performed at end-diastole, the onset of the ECG Q wave. Measurement is made from maximal medial to lateral measurement in the right ventricle

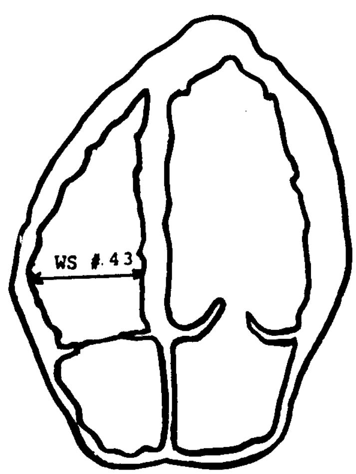


Figure 14, WS #43

- Right Ventricular Area Diastole (Fig. 15, WS #44)

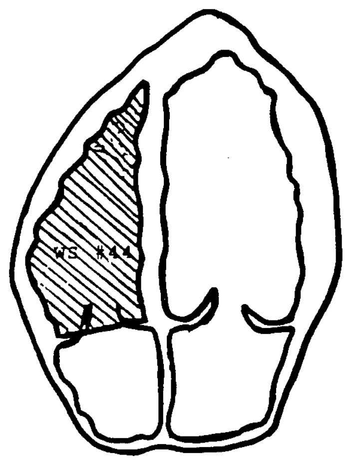


Figure 15, WS #44

DOPPLER MEASUREMENTS

Doppler measurements are made utilizing three modalities:

Pulsed-wave Doppler (PW)

Continuous-wave Doppler (CW)

Color-flow imaging (CFI)

When measurements of velocity are to be obtained, we recommend that the beam be aligned as parallel as possible to the direction of blood flow. When measuring the left ventricular outflow tract and pulmonary artery velocity, the sample volume for pulsed-wave Doppler measurement should be positioned in the plane of the valve ring. Special attention should be given to recording three consecutive heart beats with the maximal velocity obtained recorded. These velocities should reflect the appropriate spectral envelope. The recording of the Doppler studies should be done at 100 mm/sec so appropriate systolic time intervals can be measured. The study of systolic time intervals in the Doppler mode requires a precisely defined ECG Q wave. The following Doppler measurements are required.

AORTIC FLOW

Aortic flow is measured with CW Doppler, most typically with 2-D guidance in the apical 5-chamber view. Aortic flow can also be measured from the suprasternal notch c right parasternal border (Fig. 16).

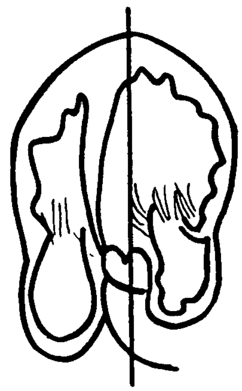


Figure 16

- Peak Aortic Velocity (Fig. 17, WS #45) CW Doppler measurement

Figure 17, WS #45

- Left Ventricular Pre-Ejection Time, Left Ventricular Ejection Time, Left Ventricular Acceleration Time (Fig. 18, WS #46, #47, #48)

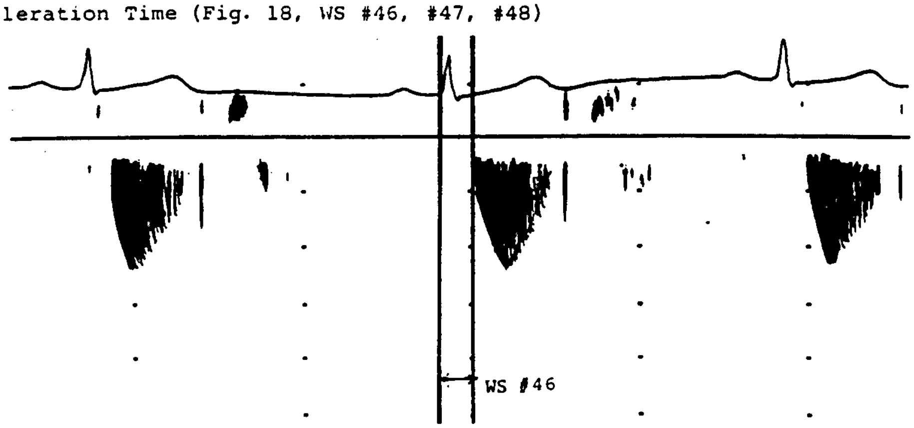


Figure 18, WS #46

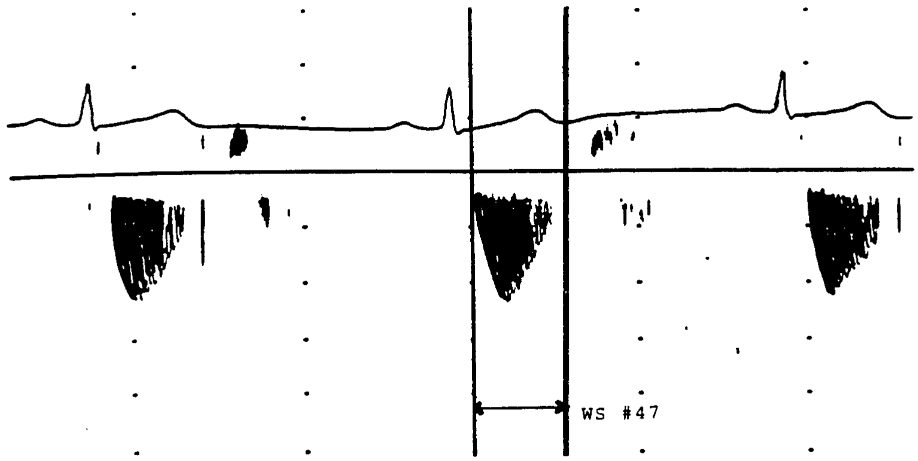


Figure 18, WS #47

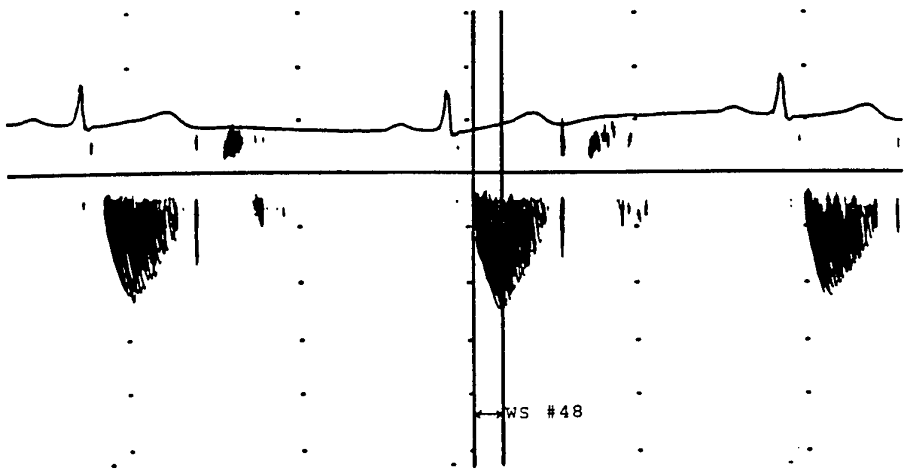


Figure 18, WS #48

- Aortic Insufficiency (WS #49)

Aortic insufficiency should be graded by CFI utilizing the apical 5-chamber view, parasternal long-axis view, and apical 2-chamber view. Aortic insufficiency shall be graded as minimal, mild, moderate, or severe. Minimal aortic insufficiency is defined when the insufficiency jet is seen just behind the aortic valve. Mild aortic insufficiency is defined by the presence of a jet extending back across the aortic valve but not past the tips of the mitral leaflets. The width of the aortic insufficiency jet should be less than 25% of the left ventricular outflow tract. Moderate aortic insufficiency is defined as an insufficiency jet extending past the tips of the mitral valve but encompassing less than 50% of the left ventricular cavity volume. The width of this aortic insufficiency jet should be greater than 25% but less than 50% of the left ventricular outflow tract. Severe aortic insufficiency is defined when the jet reaches back and encompasses greater than 50% of the left ventricular cavity volume, and when the jet takes greater than 50% of the left ventricular outflow tract in width.

PULMONARY FLOW

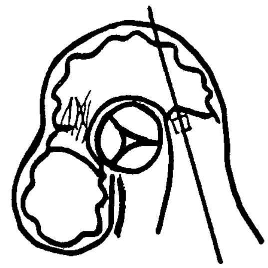


Figure 19, WS #50

- Peak velocity (Fig. 20, WS #50)

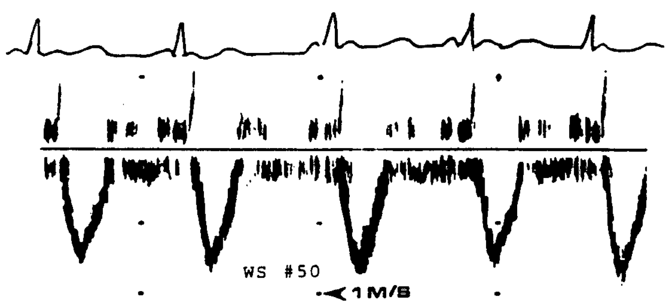


Figure 20, WS #50

- Right Ventricular Pre-Ejection Time, Right Ventricular Ejection Time, Right Ventricular Acceleration Time (Fig. 21, WS #51, #52, #53)

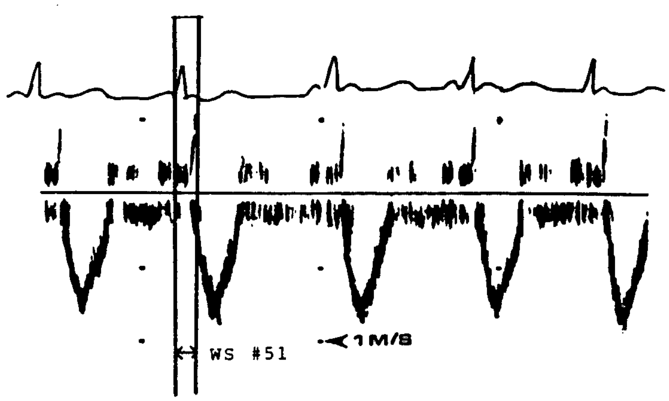


Figure 21, WS #51

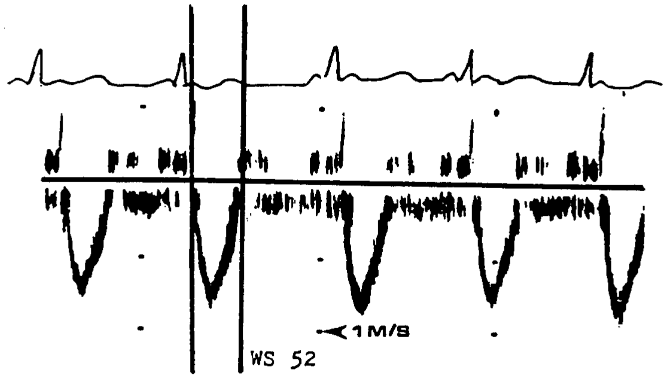


Figure 21, WS #52

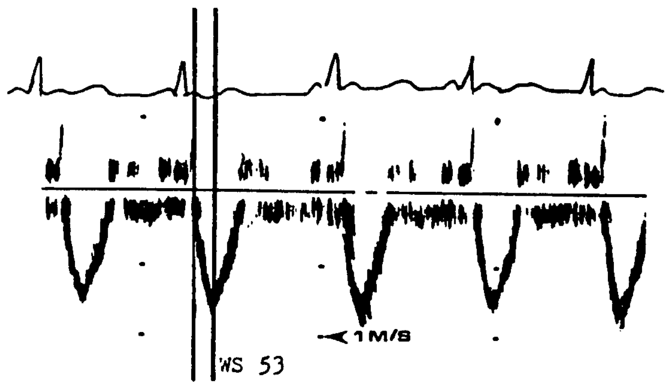


Figure 21, WS #53

- Pulmonary insufficiency shall be noted and graded when there is a jet illustrated by CFI extending back from the pulmonic valve into the right ventricular outflow tract. If this is not noted, then there is no pulmonary insufficiency. Pulmonary insufficiency shall be graded as minimal, mild, moderate, or severe. Minimal pulmonary insufficiency is defined as a small jet or "candle flame"-appearing image flowing back into the right ventricular outflow tract but involving a minimal area as compared to the outflow tract area. Mild pulmonary insufficiency is defined as a well-defined jet, though not reaching 25% of the area of the outflow tract. Moderate pulmonary insufficiency is defined as a jet encompassing 25%-50% of the right ventricular outflow tract area. Severe pulmonary insufficiency is defined as a jet encompassing greater than 50% of the right ventricular outflow tract area.

MITRAL VALVE

- Peak Velocities for the E and A Point (Fig. 22, WS #55, #56)

E and A point velocities are measured with PW Doppler with the sample volume placed at the tips of the mitral leaflets during diastole. It is of utmost importance that the sample volume be placed right at the mitral leaflet tips, in diastole, in the apical 4-chamber view.

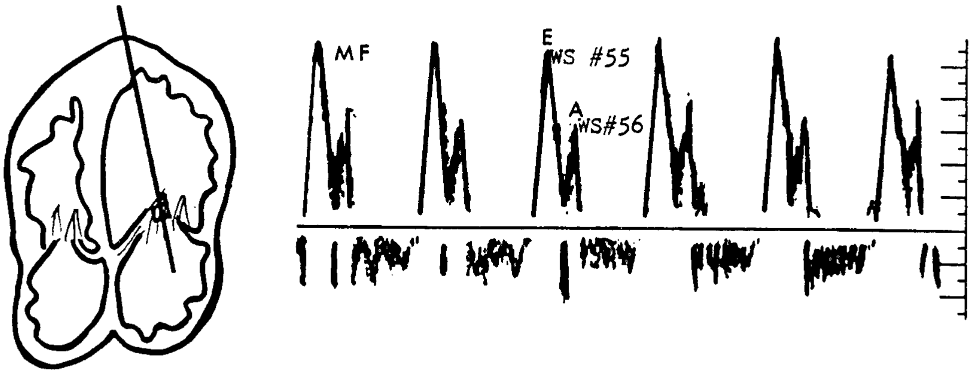


Figure 22, WS #55, #56

- Mitral Regurgitation (WS #57)

Mitral regurgitation should be graded using CFI. Standard views for grading mitra regurgitation are the parasternal long-axis view, apical 4-chamber view, and apical 2-chamber view. Minimal mitral regurgitation is noted when the regurgitant jet just crosses the mitral valve during systole. Mild mitral regurgitation is defined as a regurgitant jet encompassing 20%-40% of the left atrial area. Severe mitral regurgitation is defined as a regurgitant jet which encompasses greater than 40% of the left atrial area.

TRICUSPID VALVE

- Peak Velocity E, Peak Velocity A (Fig. 23, WS #58, #59)

The peak E and A point velocities for the tricuspid valve shall be measured in th apical 4-chamber view with PW Doppler. The PW sample volume shall be placed at the ti of the tricuspid leaflets during diastole. Special attention must be given to the placement of the sample PW Doppler sample volume in order to obtain the correct right ventricular inflow tract E and A point velocities.

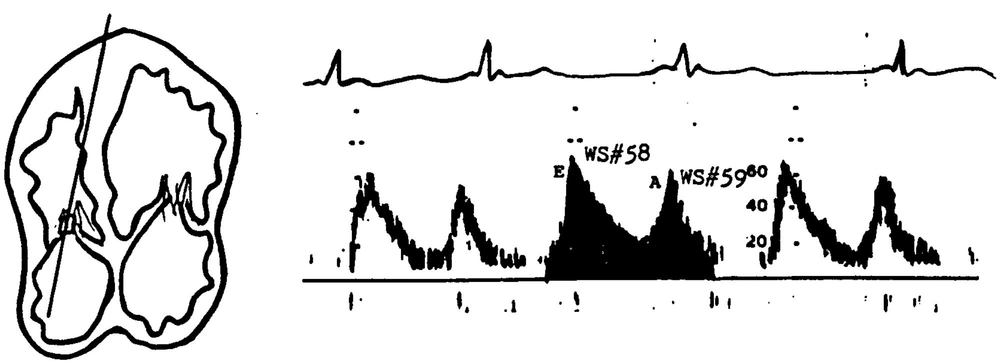


Figure 23, WS #58, #59

- Tricuspid Regurgitation (WS #60)

The definitions of severity for tricuspid regurgitation are identical to the def: nitions of severity for mitral regurgitation. Please refer to that explanation above

QUALITATIVE ECHOCARDIOGRAPHIC ASSESSMENT

- Mitral Valve Prolapse (Fig. 24, WS #65, #70)

The echocardiographic diagnosis of mitral valve prolapse (MVP) will be made by bi-directional criteria when both leaflets together, either leaflet alone, or parts of either leaflet cross the annular plane during systole, when viewed in the parasternal long-axis view. M-mode criteria require that 2 mm of late systolic hammocking be present; 3 mm of pansystolic hammocking is diagnostic of MVP when 2-D confirmation (as described) is made. If 2-D criteria for the diagnosis of MVP are not met, M-mode pan-systolic hammocking alone is not sufficient to diagnosis MVP.

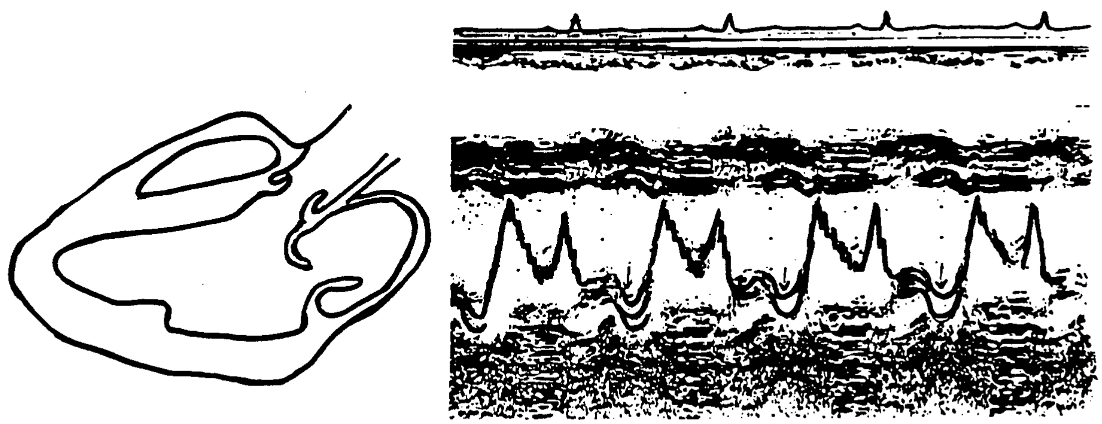


Figure 24, WS #65, #70

- Walls Hypokinetic Segment, Dyskinetic Segment (Fig. 25, WS #83, #84)

If a wall motion abnormality is present, please refer to the appropriate wall segment and designate this wall segment appropriately.

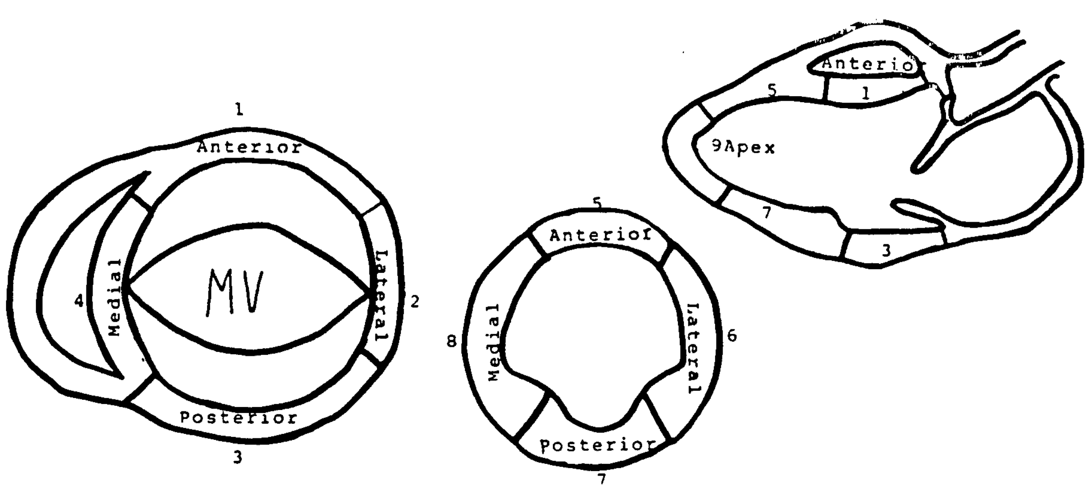


Figure 25, WS #83, #84

ANNEX D

ANNEX D: AIRCRAFT

Type A - High Sustained G (HSG) Aircraft [> 7G > 15 Secs]
Type B - Non-HSG Fighter, Bomber or Trainer Aircraft
Type C - Transport, Patrol or RW Aircraft

CODE NO	NAME	TYPE
2.	A3	B
3.	A4	B
4.	A5	B
5.	A6	B
6.	A7	B
7.	A10	B
8.	Alize	B
9.	Alpha Jet	B
10.	AMX	B
11.	Andover	C
12.	AT 37 A37/T37	B
13.	Avio Jet	B
14.	Atlantic	C
15.	Azor	C
16.	B 1	C
17.	B 52	C
18.	B 57-66	C
19.	B707-C135, 137, E3	C
20.	B727 - C 22	C
21.	B 737 - T 43	C
22.	B 747 - E 4	C
23.	BA 146	C
24.	BAC 111	C
25.	Belfast	C
26.	Buccaneer	B
27.	Buffalo	C
28.	C 1 - Tracker	C
29.	C 5	C
30.	C 9 - DC 9	C
31.	C 47, 117 - Dakota	C
32.	C 101	B
33.	C 118 - DC 6- DC 7	C
34.	C 119	C
35.	C 123	C
36.	C 124	C
37.	C 140 - Jet Star	C
38.	C 141	C
39.	C 212 -	C
40.	Cambera	B
41.	Challenger	C
42.	Caribou	C
43.	CF 100	B
44.	CL 215	C
45.	CP 107	C
46.	CT 39 - C 20 - C21	C
47.	DC 8	C
48.	Devon Sea	C
49.	Draken	A
50.	E 3 - Hawkeye	C
51.	Etendard 4	B
52.	F 4 Phatom	B
53.	F 5 Tiger	A
54.	F 8 Crusader	B
55.	F 14	A
56.	F 15	A
57.	F 16	A
58.	F 18	A
59.	F 84	B
60.	F 86	B
61.	F 100	B
62.	F 101	B
63.	F 102	B
64.	F 104	B
65.	F 105	B
66.	F 106	B
67.	F 111	B
68.	Falcon 10, 20, 50, 900	C
69.	Fouga	B
70.	Fouga Magister	B
71.	G 91	B
72.	G 222	C
73.	Gnat	A
74.	Harrier-Sea	B
75.	Hawk	A
76.	Hercules C 130	C
77.	HS 125	C
78.	Hunter	B
79.	Jaguar	B
80.	KC 97	C
81.	Lightning	A
82.	M 326	C
83.	M 339	C
84.	Mirage 2000	A
85.	Mirage 3	A
86.	Mirage 4	A
87.	Mirage 5	B
88.	Mirage F1	A
89.	MS 760	
90.	Mystère	C
91.	N 2501	C
92.	N 262	C
93.	Nimrod	C
94.	P 3 - Orion	C
95.	P 166	C
96.	PD 808	B
97.	Pembroque	C
98.	S 3 - Viking - C 2A	C
99.	S 211	
100.	SMB 2	
101.	Super Etendard	B
102.	T 33	B
103.	Tornado	A
104.	Transall - C 160	C
105.	Tutor	B
106.	VC 10	C
107.	Venom	B
108.	Vulcan	C
109.	Other HSG	A
110.	Other B (egT38)	B
111.	Other C 'S	C
112.	Helicopter	C

APPENDICES A-C

Appendices A-C are included to present the database results in greater detail for the interested reader. This information is not necessary for an understanding of the results of this project which are presented and discussed earlier in this publication. This information is offered to the interested reader who would like a more detailed view of the database.

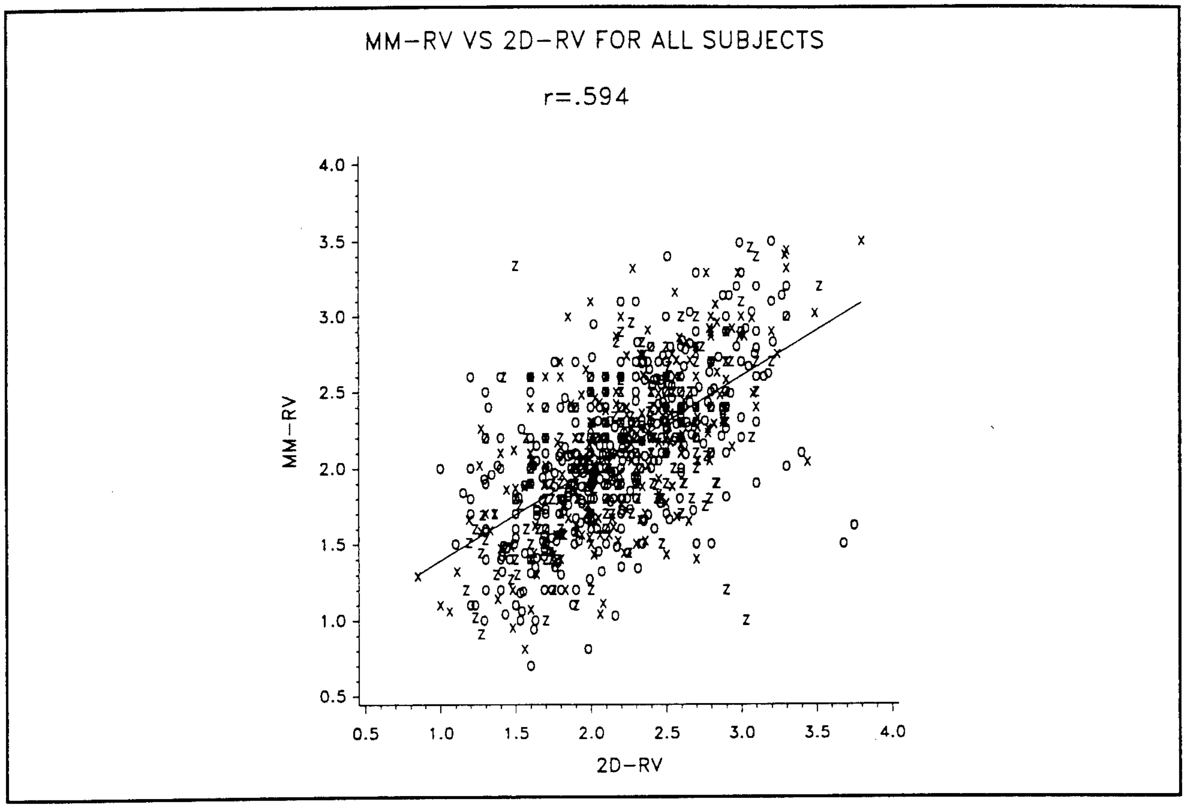
Appendix A: This section presents all of the measurements of the 16 echocardiographic parameters from the entire prospective database displayed in eight scattergrams. The scattergrams provide the reader with a visual display of all the measured parameters further divided into the three pilot subtypes of XX, ZZ and all other pilot types.

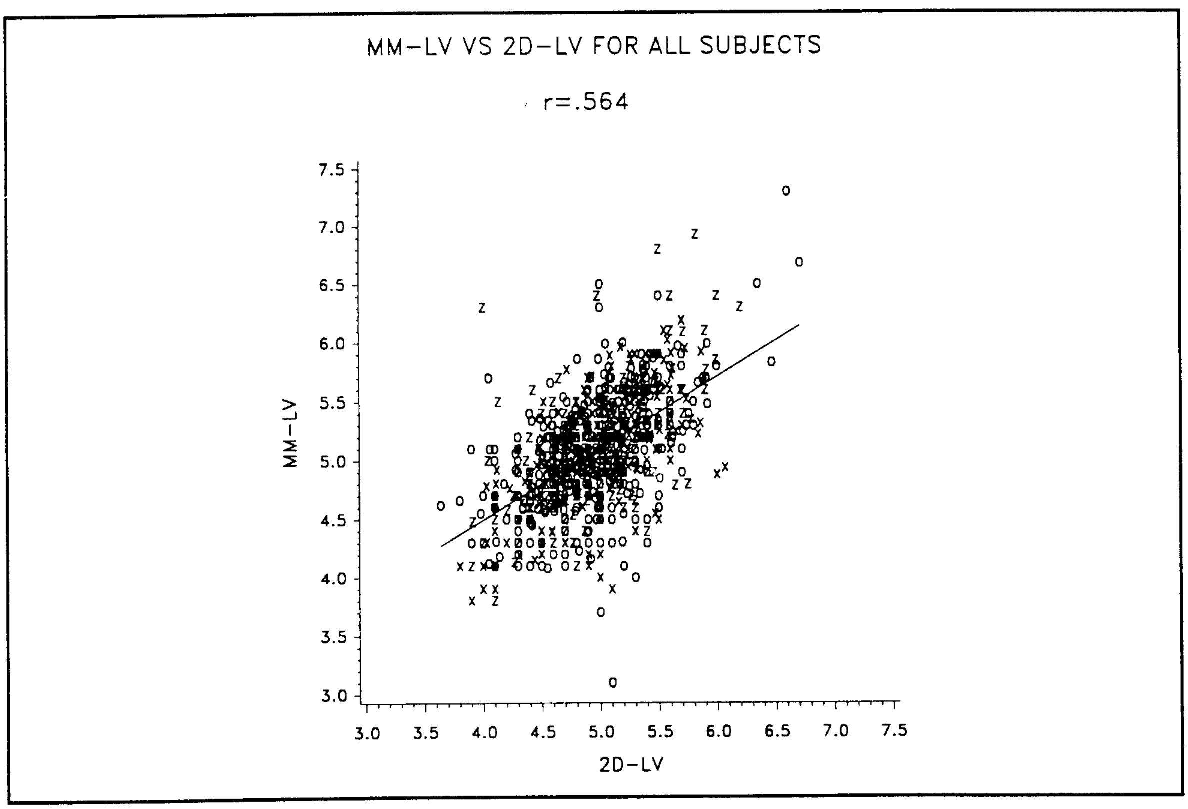
Appendix B: Although analysis of the database revealed no significant difference in the measured echocardiographic parameters between XX and ZZ pilots, a dose-related effect of high performance (XX) flying might have been missed. Such an effect was considered but was found not to be present. Appendix B displays the results of this analysis in several graphs. Adjusted means for each echocardiographic parameter were calculated for each decile of flying hours in XX and ZZ pilots. These "by decile" means demonstrate no dose-related effect of XX versus ZZ flying for any of the echocardiographic parameters.

Appendix C: The demographic data and the echcocardio-graphic measurements are presented in graphs by country and by pilot type, XX versus ZZ, within each country.

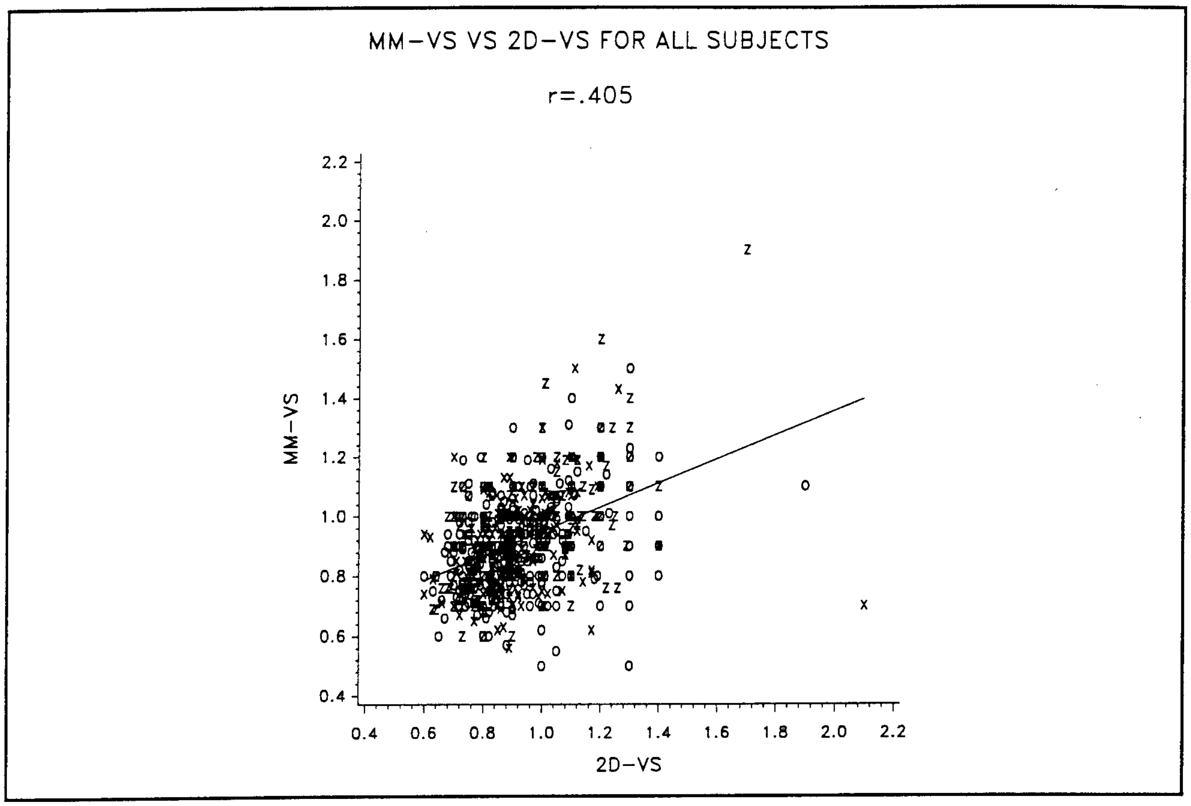
APPENDIX A

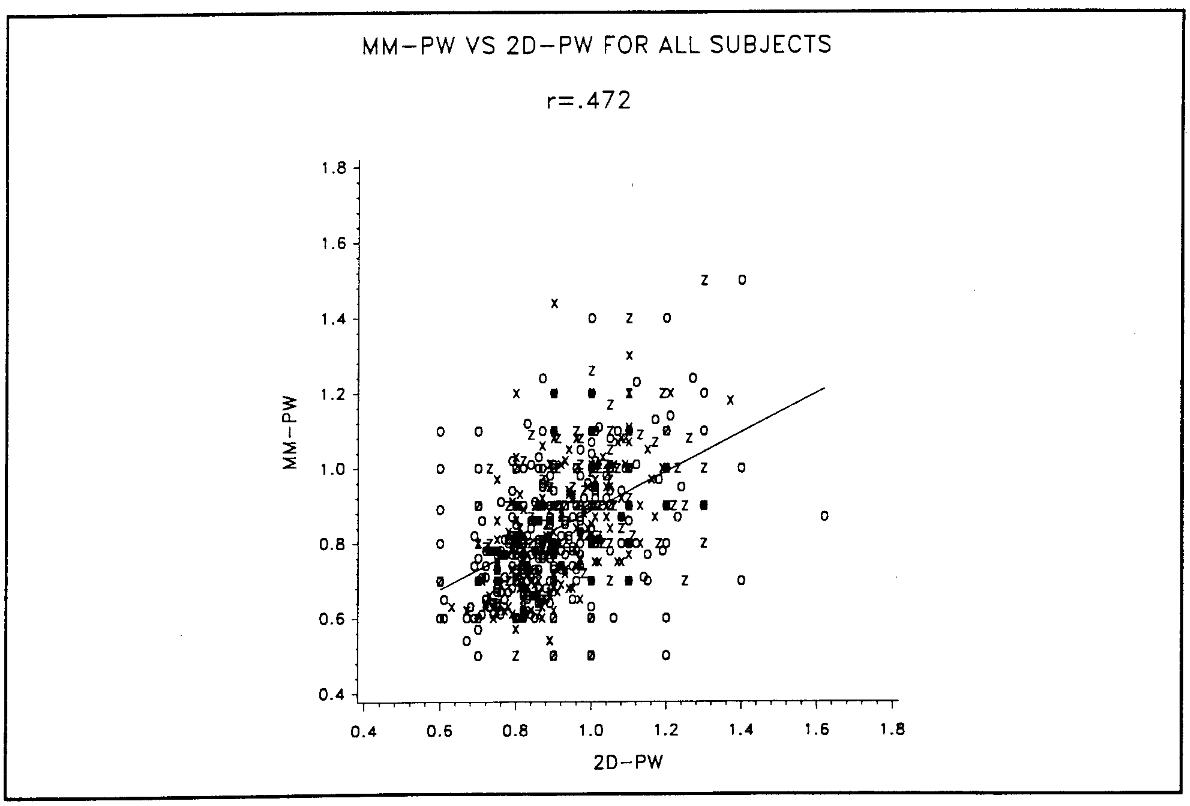
Appendix A presents the echocardiographic parameters in greater detail in the form of scattergrams. Each scattergram displays two related echocardiographic parameters on the X and Y axes, such as MM-RV and 2D-RV. Additionally, RVMAX is plotted against RV-AR and MVE/A is plotted against TVE/A. In each scattergram, all of the measurements from the prospective database are displayed. Measurements from XX pilots are shown as X, from ZZ pilots as Z and from all other pilot categories as O. These scattergrams allow the reader to see several things: (1) the degree of variability and the range of values of each measurement for each of the three pilot categories XX, ZZ and "other", (2) the degree of agreement between related M-mode and 2D measurements, and (3) the overlap between the values in the three pilot categories. This visual display of the database reinforces the findings reported - there is no significant effect on these measured parameters by pilot category.



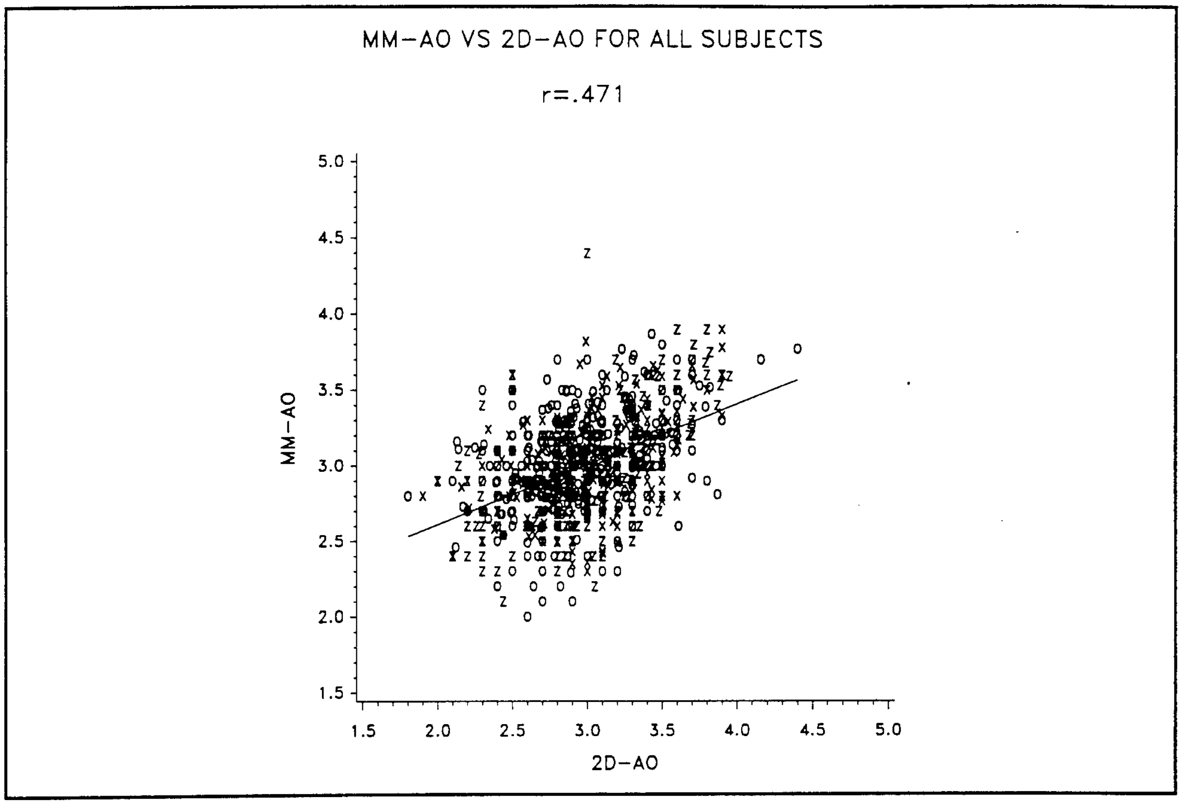


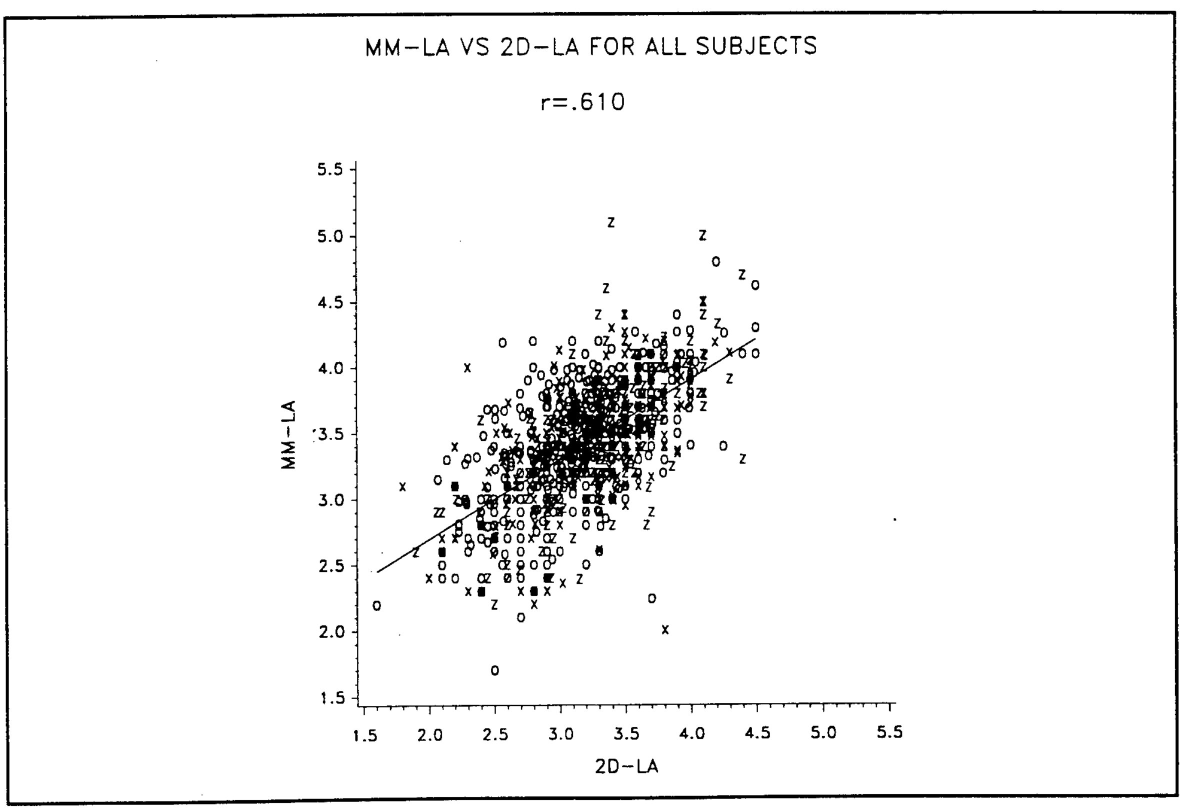
Legend: 'X' = XX Pilot, 'Z' = ZZ Pilot, 'O' = All others



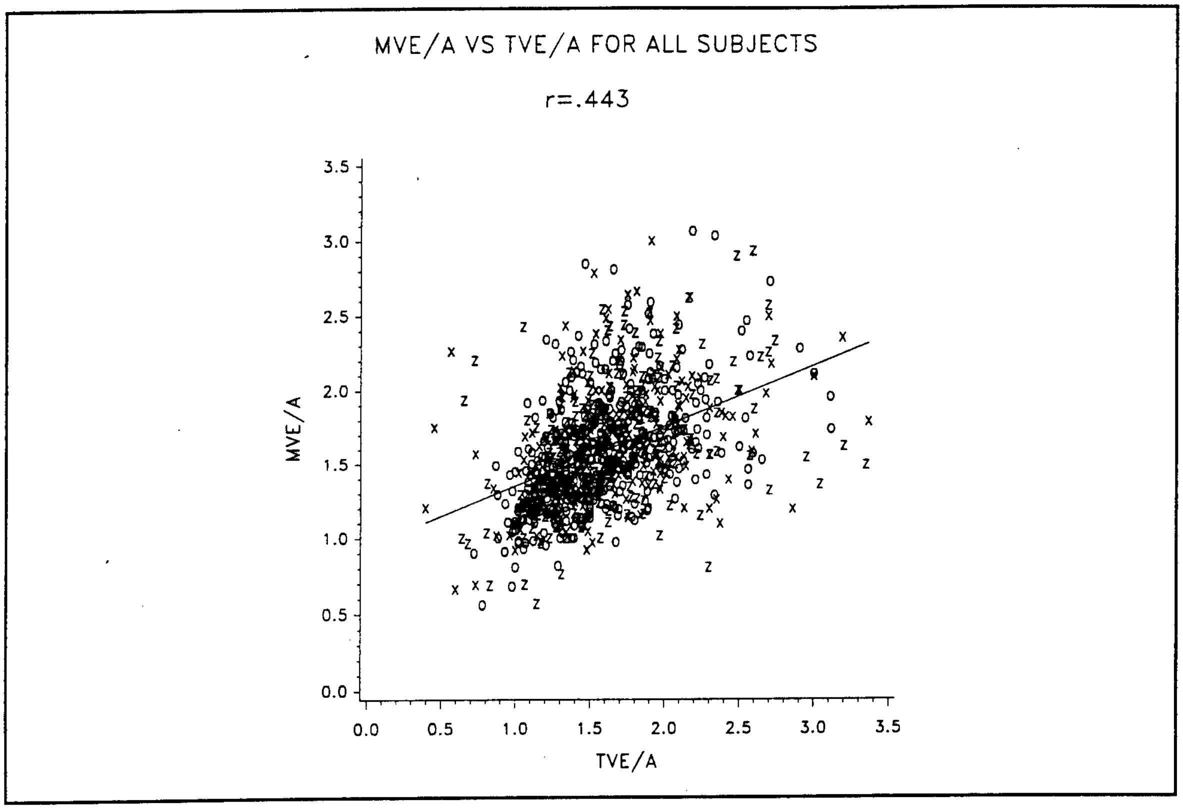


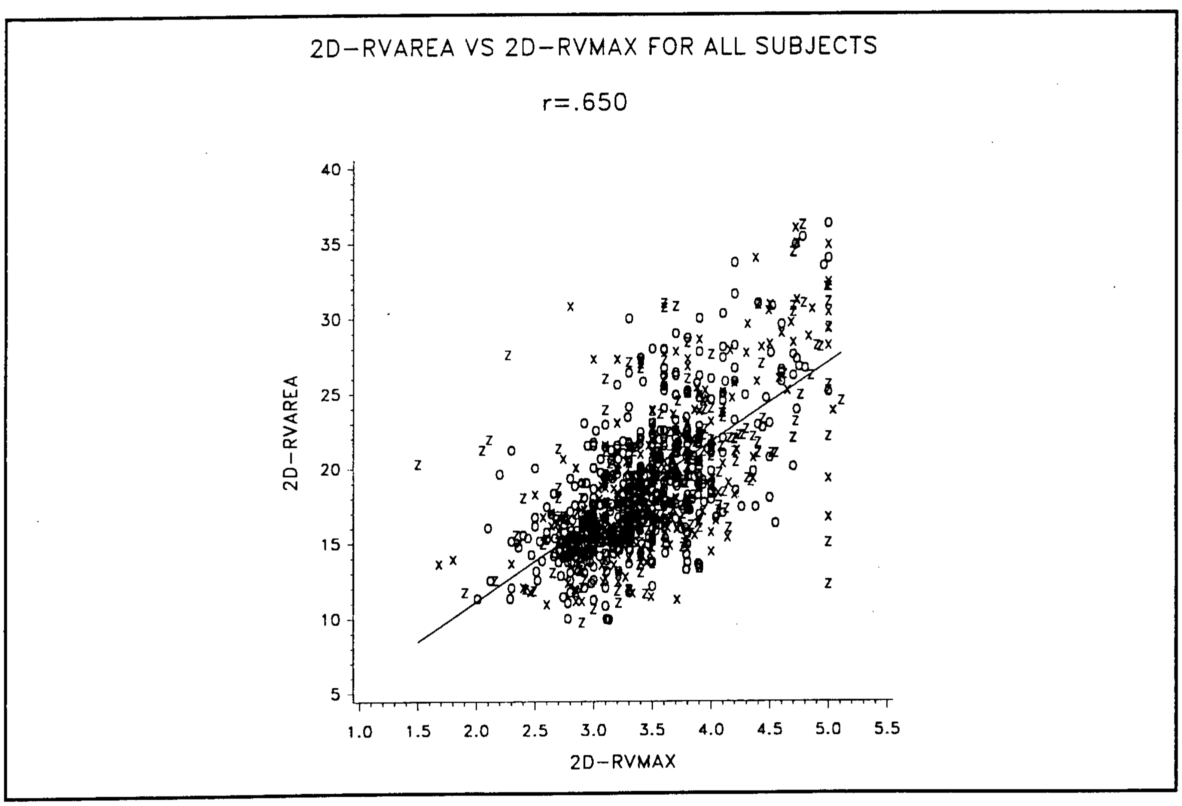
Legend: 'X' = XX Pilot, 'Z' = ZZ Pilot, 'O' = All others





Legend: 'X' = XX Pilot, 'Z' = ZZ Pilot, 'O' = All others





Legend: 'X' = XX Pilot, 'Z' = ZZ Pilot, 'O' = All others

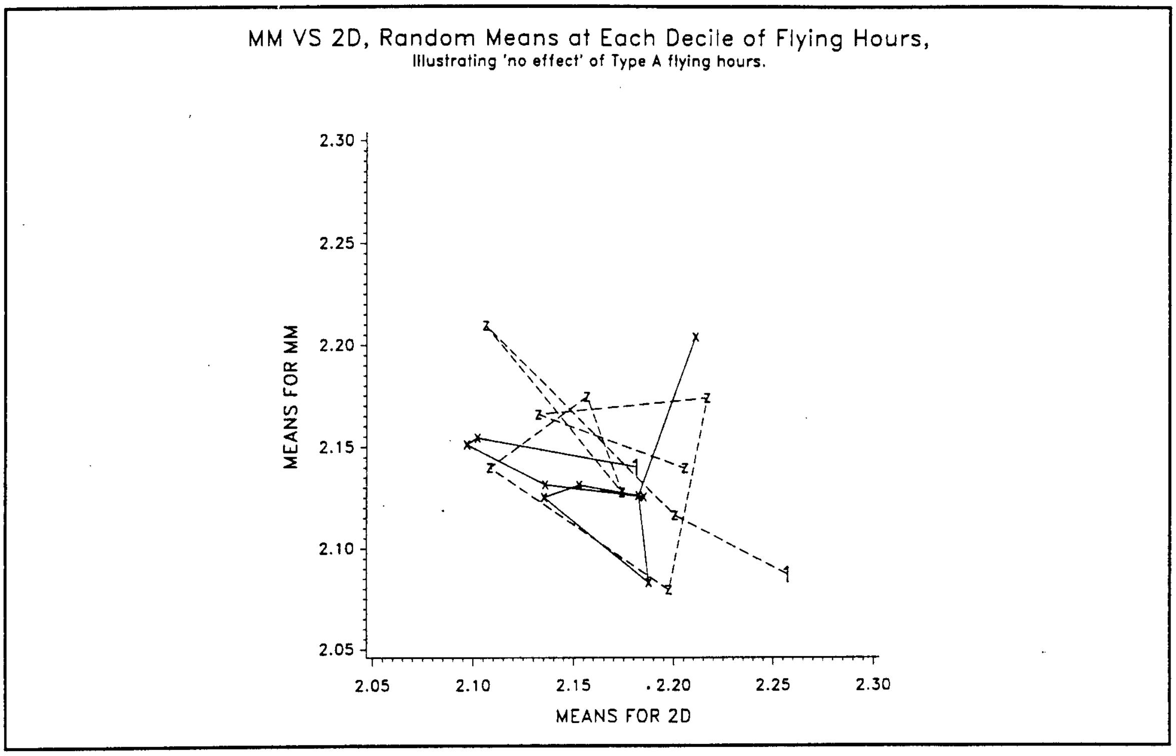
APPENDIX B

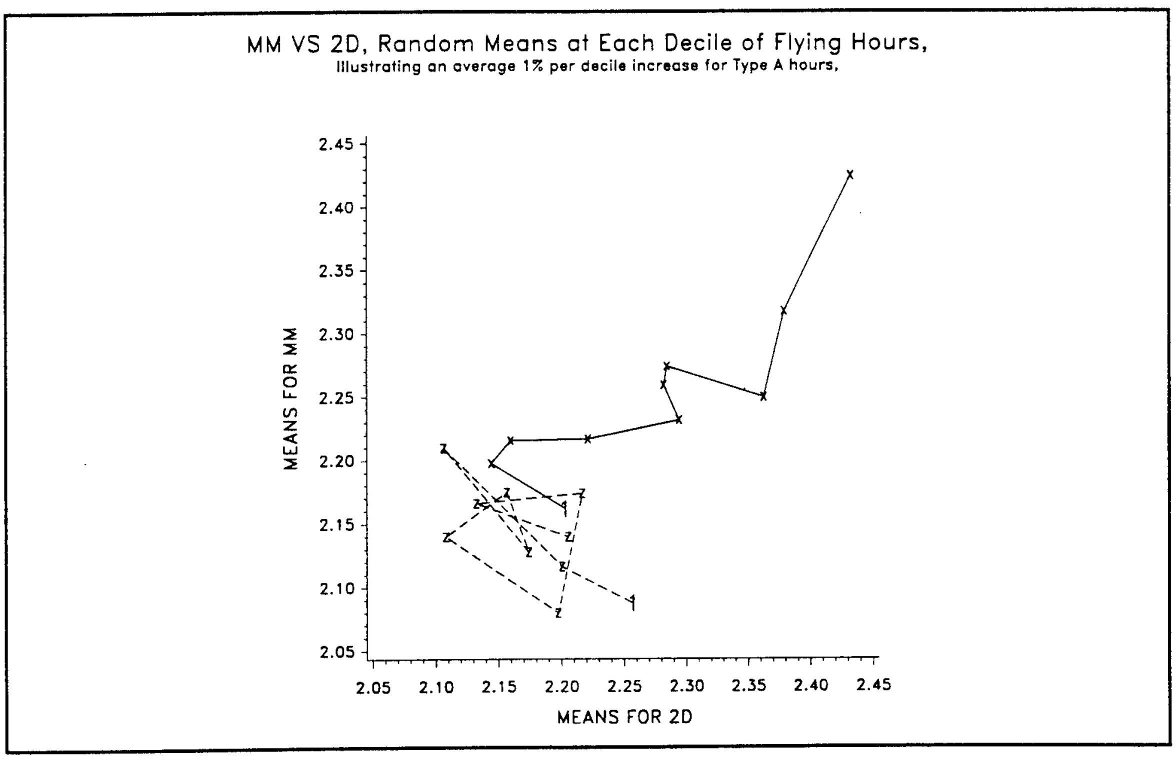
The results of this project demonstrate no independent effect of high performance (XX) flying on the analyzed echocardiographic parameters compared to non-high performance (ZZ) flying. However, it was considered that a dose-related effect might occur and might be missed in the analysis of the entire database. To explore this possibility, the measured echocardiographic parameters were evaluated by decile of flying hours in XX versus ZZ pilots and no such dose-related effect was found. This information is displayed in graphs in Appendix B.

Adjusted means for each echocardiographic measurement were calculated for each decile of flying hours in the two pilot subtypes, XX and ZZ. Means adjusted for total flying hours, age, body surface area, smoking , exercise and country of origin were calculated with analyses of covariance. Flying hours were divided into deciles, using type A hours for XX pilots and type C hours for ZZ pilots. Age was categorized as <25, 25-29, 30-34, 35-39, 40-44, and 45+ for these analyses.

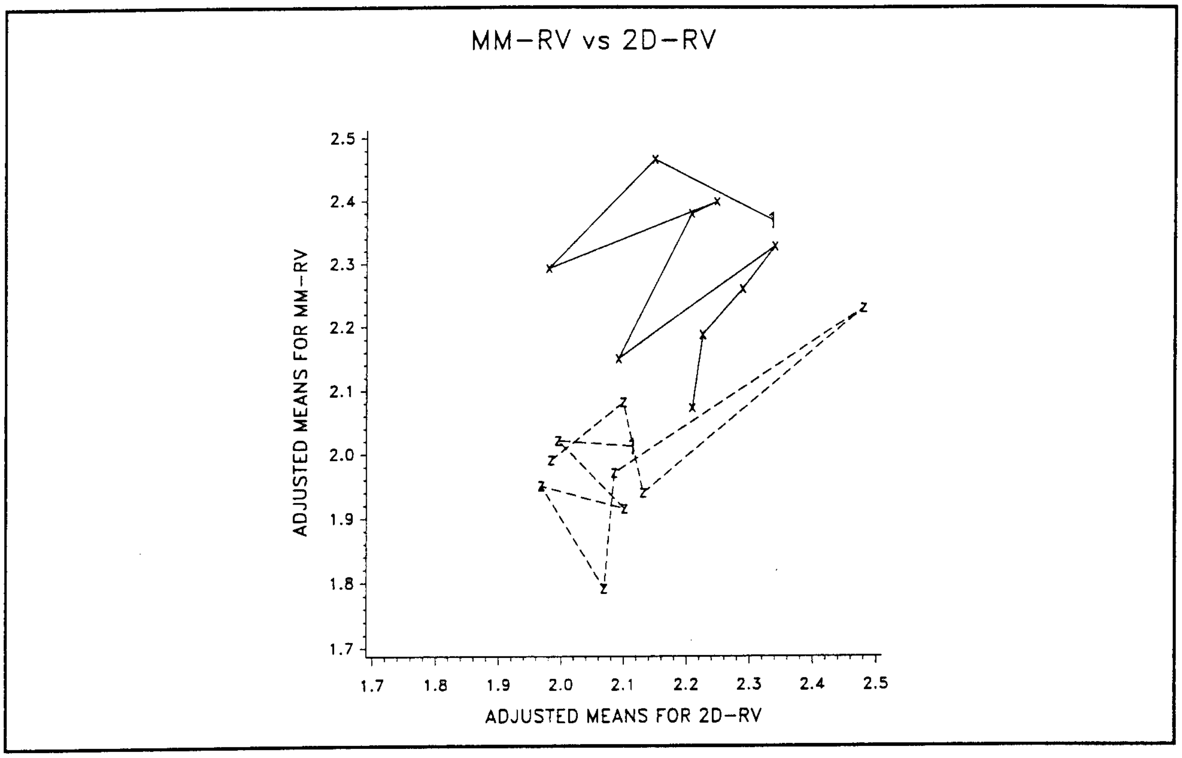
Smoking and exercise were transformed as ln (1 + pack-years) and ln (kilojoules of energy per week) to minimize the effect of skewing, as was done elsewhere in the data analysis.

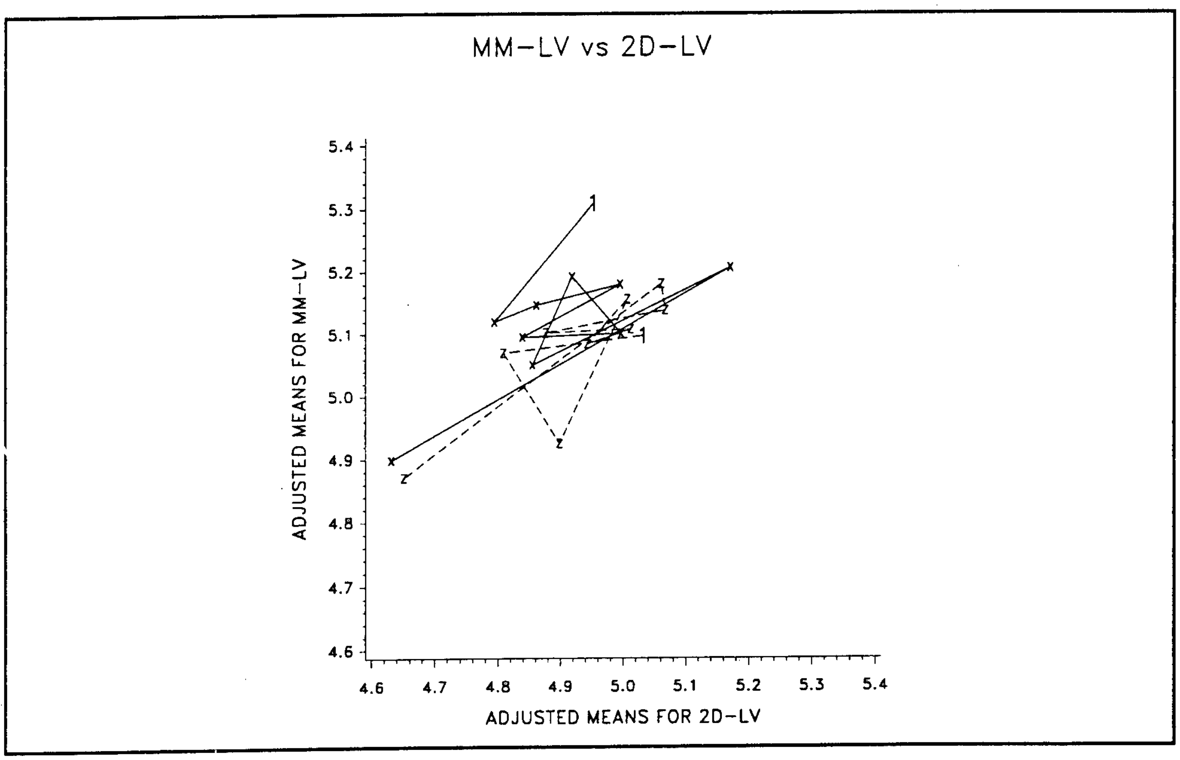
The adjusted means for each decile of XX and ZZ pilots are plotted on graphs with related echocardiographic parameters on the X and Y axes as was done in Appendix A. The first two graphs are demonstrations of how the data should appear (1) if there was no effect of type A high performance flying and (2) if there was a cumulative, dose-related 10% effect (1% per decile) of type A flying hours. The subsequent graphs display the actual data of adjusted means at each decile of flying hours. In each graph, the number "1" denotes the first decile mean value for XX or ZZ pilots. From the number "1", follow the solid lines (XX pilots) or the broken lines (ZZ pilots) to the second, third, fourth...tenth decile mean value successively. The graphs clearly show that there is no dose-related effect of type A (XX) flying on any of the analyzed echocardiographic parameters.



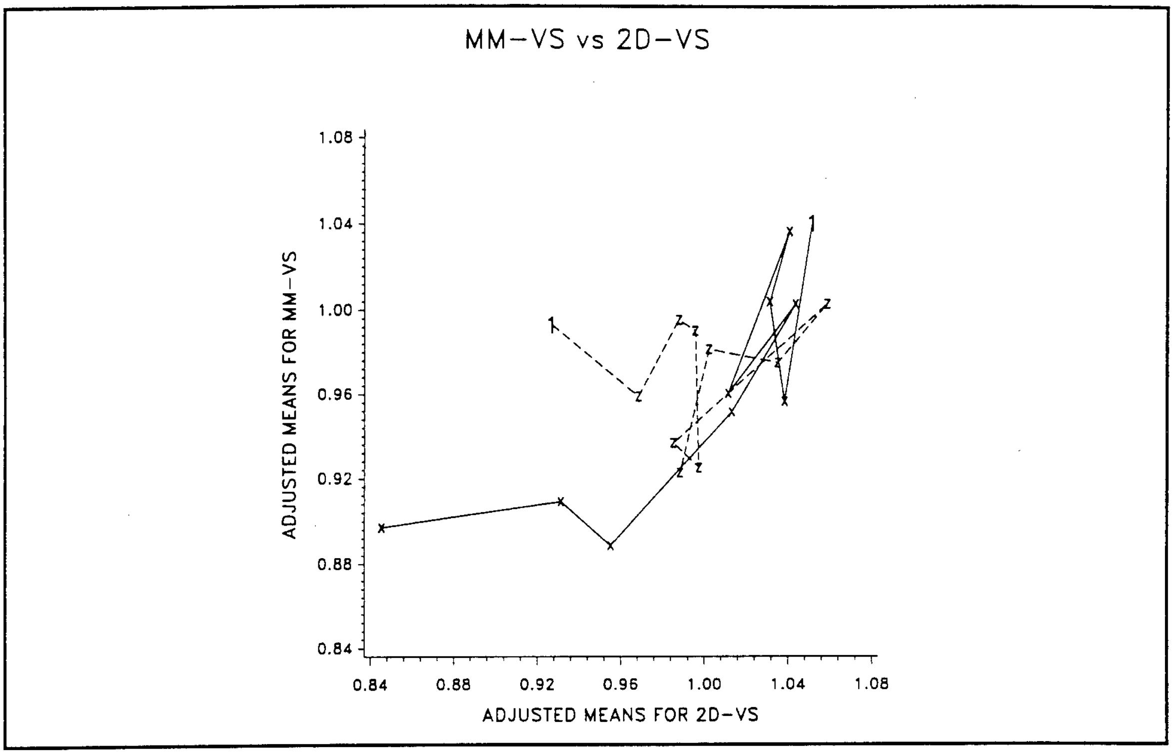


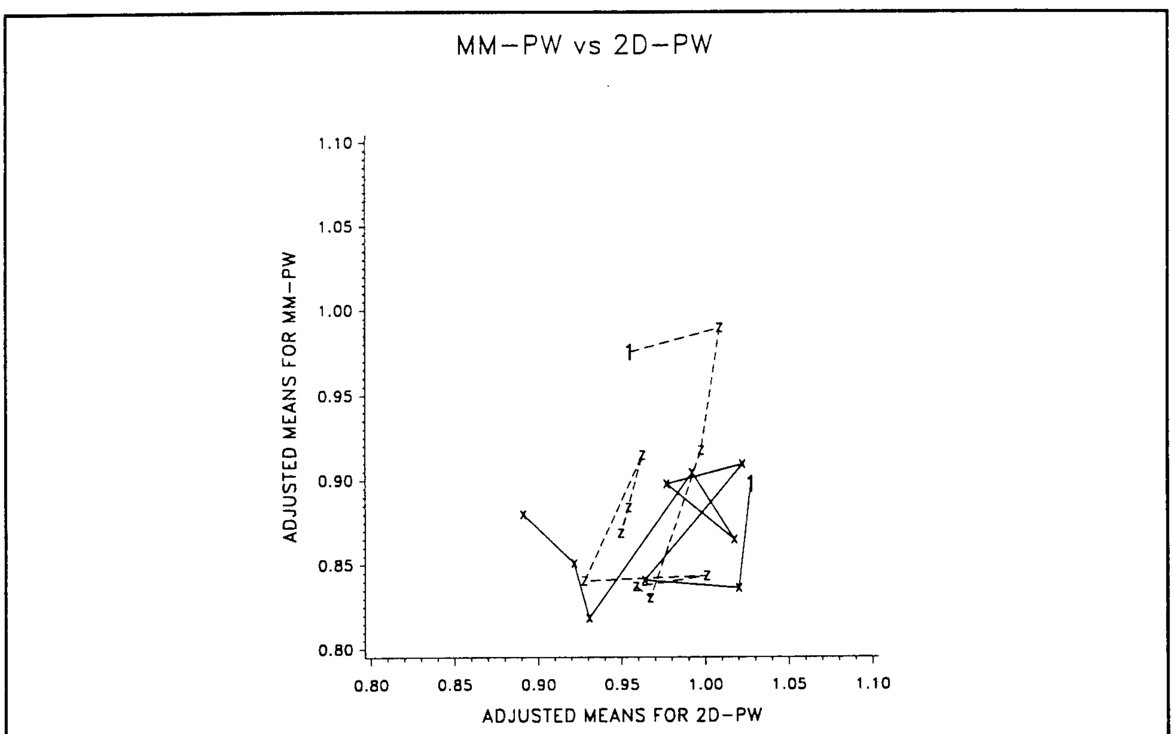
Legend: X = at each decile of Type A flying hours, Z = at each decile of Type C flying hours
1 = indicates 1st decile of Type A or C flying hours



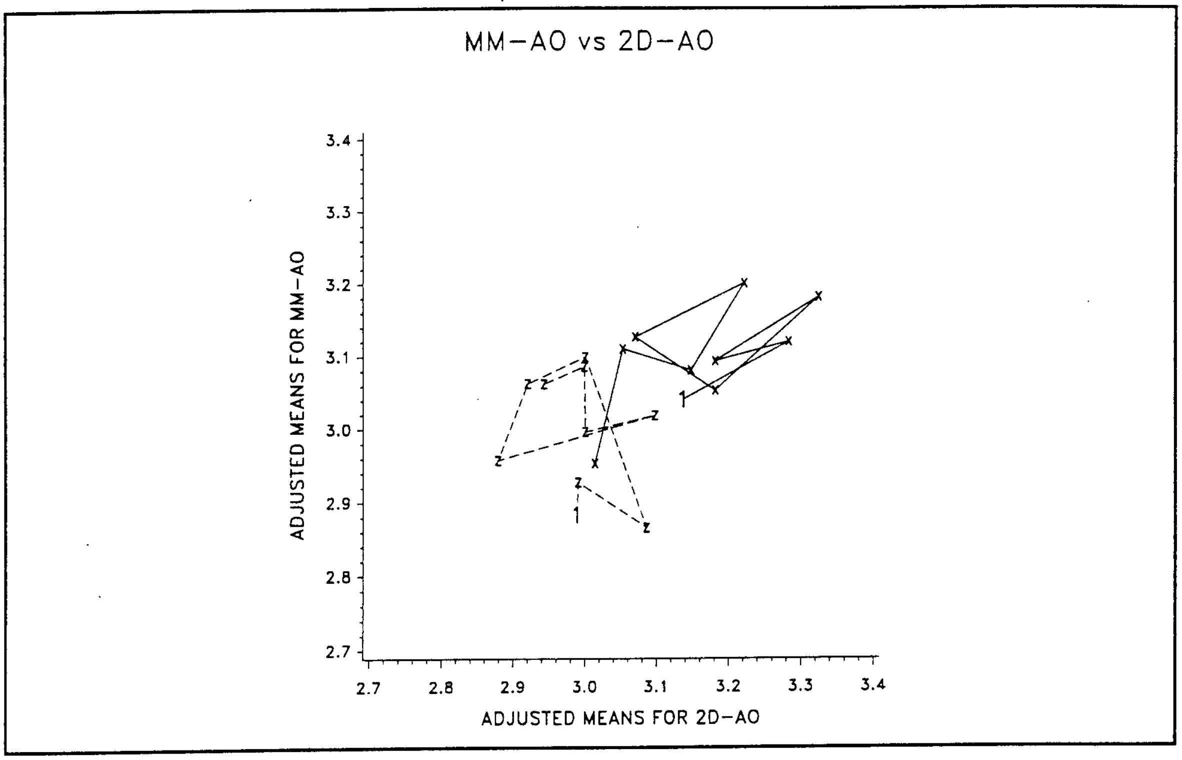


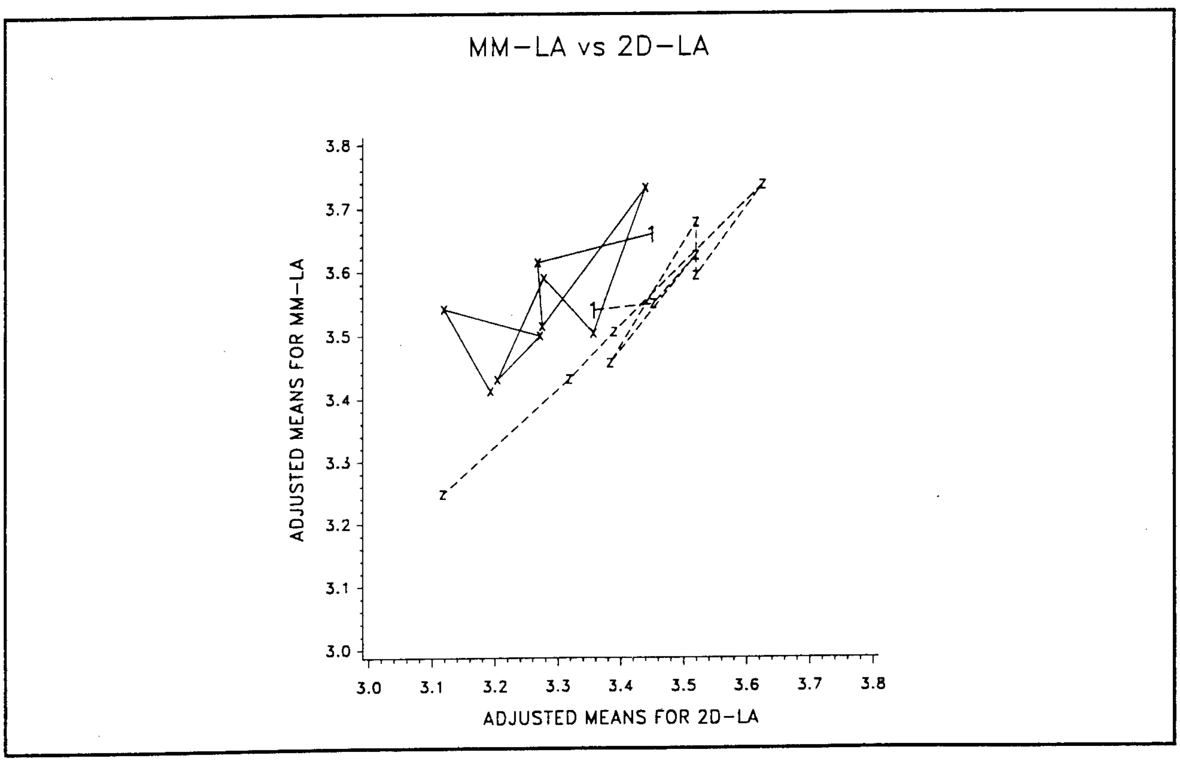
Legend: Means at each decile of flying hours are adjusted for age, BSA, Smoking, Exercise, and Country. Deciles are Type A flying hours for XX pilots and Type C flying hours for ZZ pilots. Symbols: X = XX pilots, Z = ZZ pilots, 1 = 1st decile of Type A or Type C flying hours.



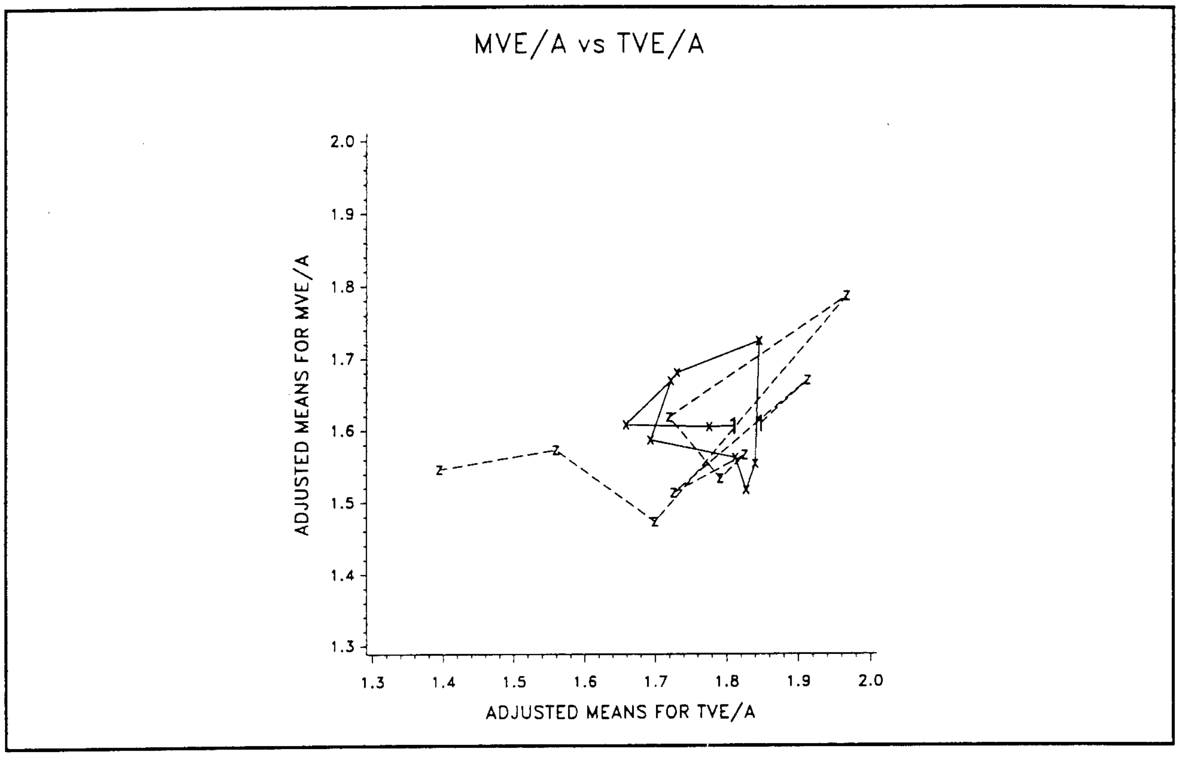


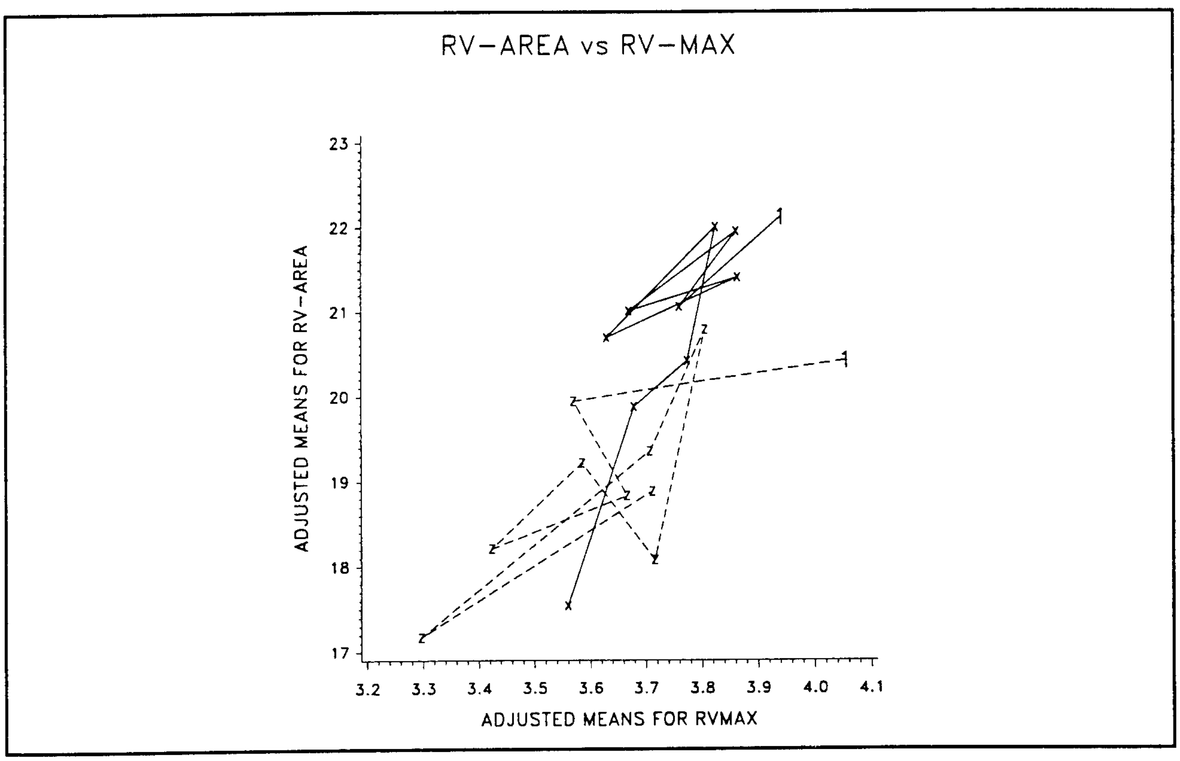
Legend: Means at each decile of flying hours are adjusted for age, BSA, Smoking, Exercise, and Country. Deciles are Type A flying hours for XX pilots and Type C flying hours for ZZ pilots. Symbols: X = XX pilots, Z = ZZ pilots, 1 = 1st decile of Type A or Type C flying hours.





Legend: Means at each decile of flying hours are adjusted for age, BSA, Smoking, Exercise, and Country. Deciles are Type A flying hours for XX pilots and Type C flying hours for ZZ pilots. Symbols: X = XX pilots, Z = ZZ pilots, 1 = 1st decile of Type A or Type C flying hours.





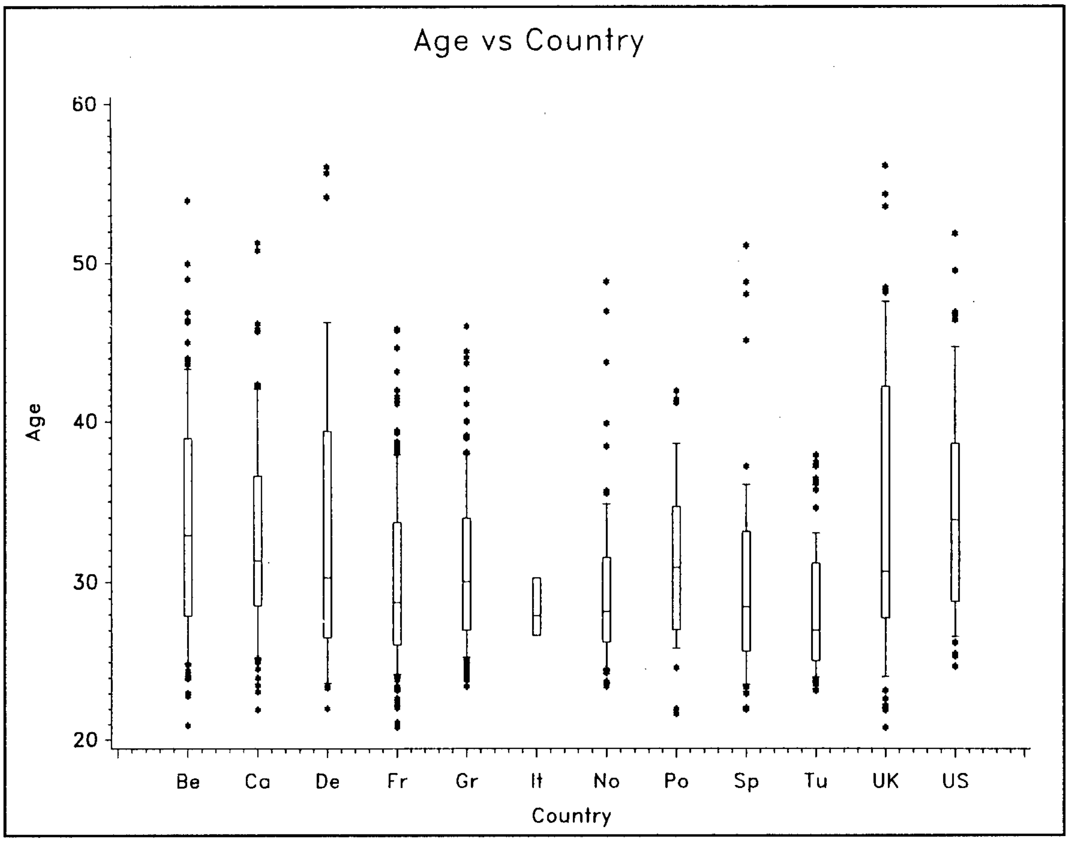
Legend: Means at each decile of flying hours are adjusted for age, BSA, Smoking, Exercise, and Country. Deciles are Type A flying hours for XX pilots and Type C flying hours for ZZ pilots. Symbols: X = XX pilots, Z = ZZ pilots, 1 = 1st decile of Type A or Type C flying hours.

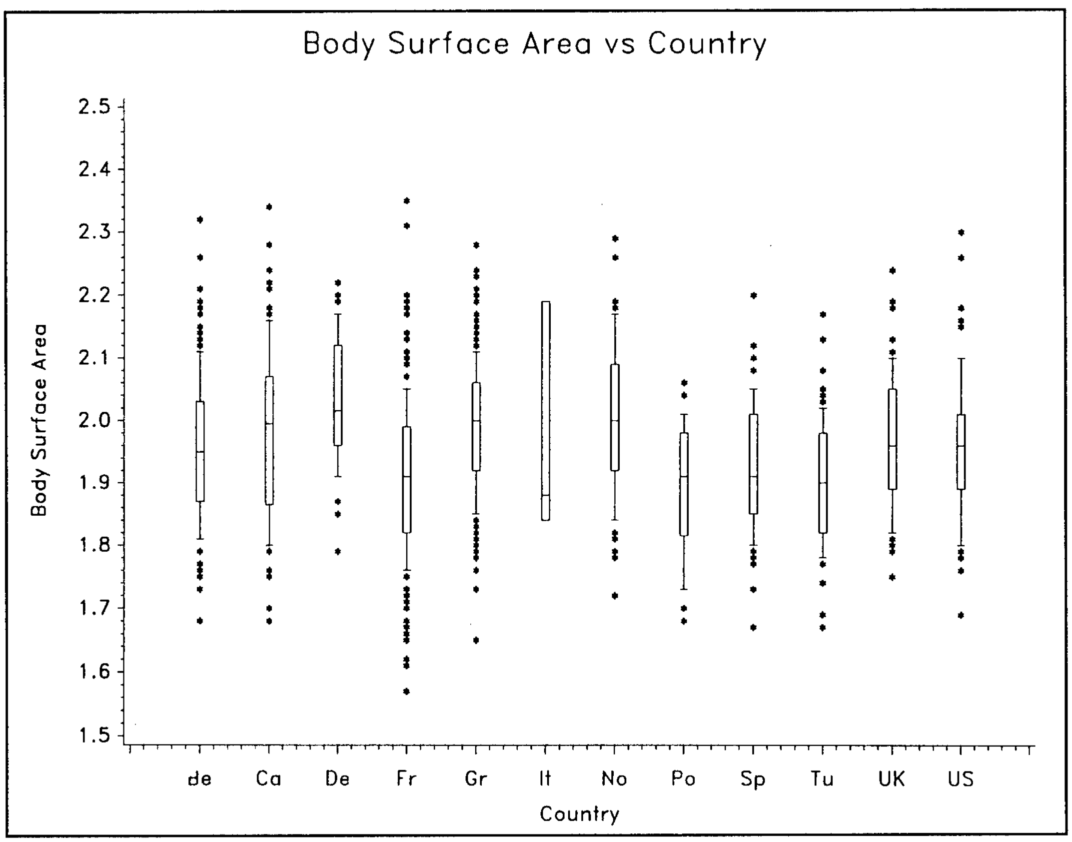
APPENDIX C

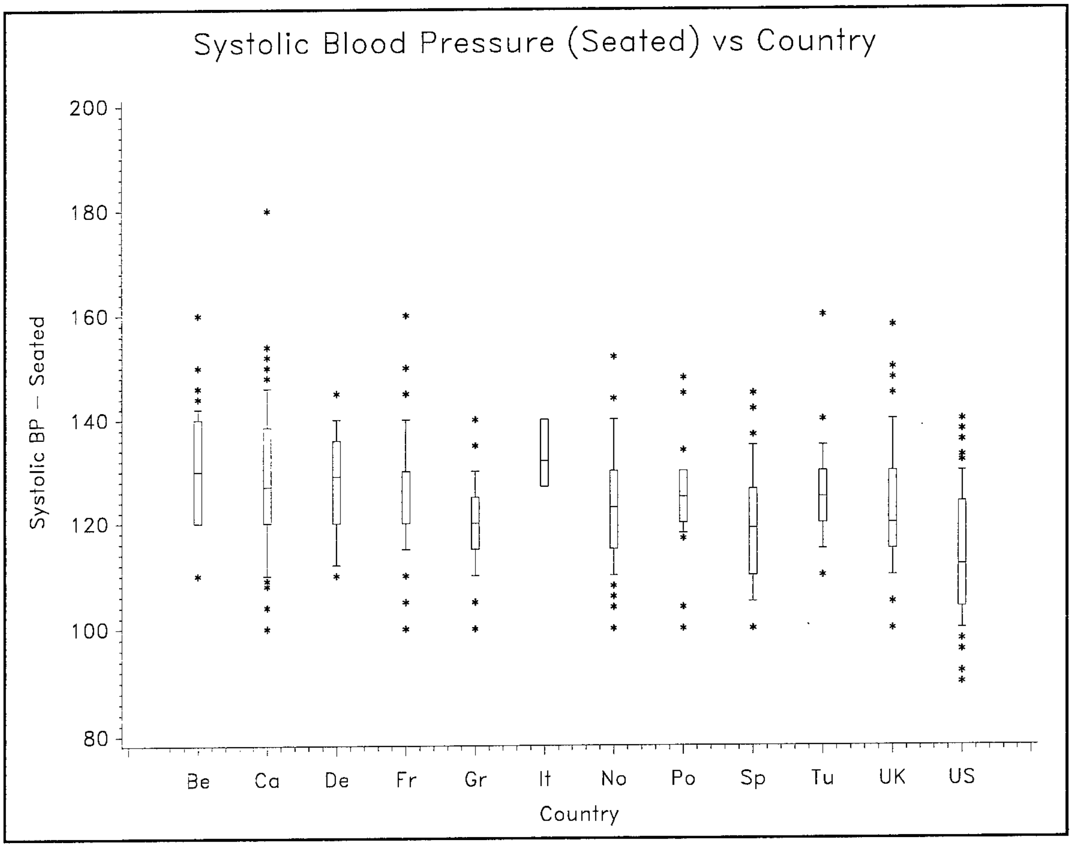
Appendix C presents the database in several graphs in more detail than was presented in the results section of this report.

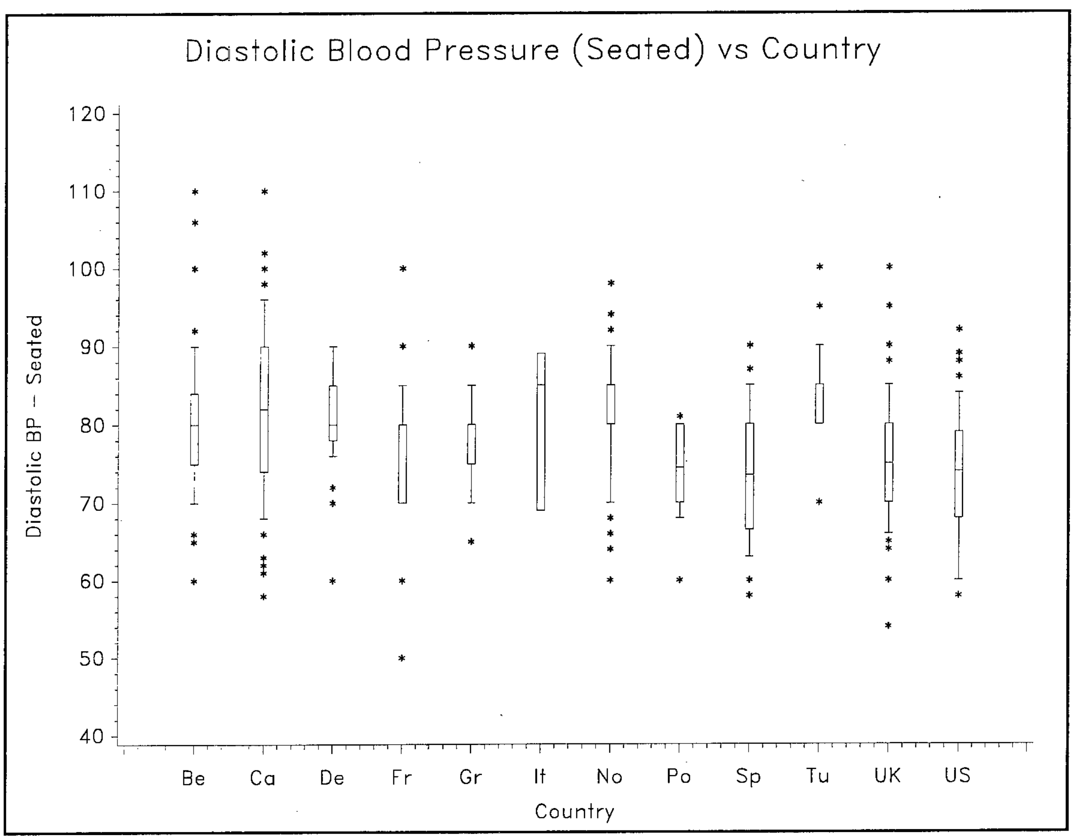
First, the demographic data is presented by country in several graphs. On the graphs, the United Kingdom is abbreviated UK and the United States is abbrevited US. Otherwise, country abbreviatons are the first two letters of the country name (BE = Belgium, CA = Canada, DE = Denmark, FR = France, GR = Greece, IT = Italy, NO = Norway, PO = Portugal, SP = Spain and TU = Turkey). As in the presentation of results earlier in this report, all pilots subtypes from the prospective database are used for the demographic data display. For each country, the graphs have a vertically oriented box. The bottom and top edges of each box are located at the sample 25th and 75th percentiles. The center horizontal line in the box is drawn at the 50th percentile (median). The vertical lines, or "whiskers", above and below the boxes are drawn from the box to the most extreme point within 1.5 interquartile ranges. An interquartile range is the distance between the 25th and 75th sample percentiles. Any value more extreme than this is marked with an asterisk (*).

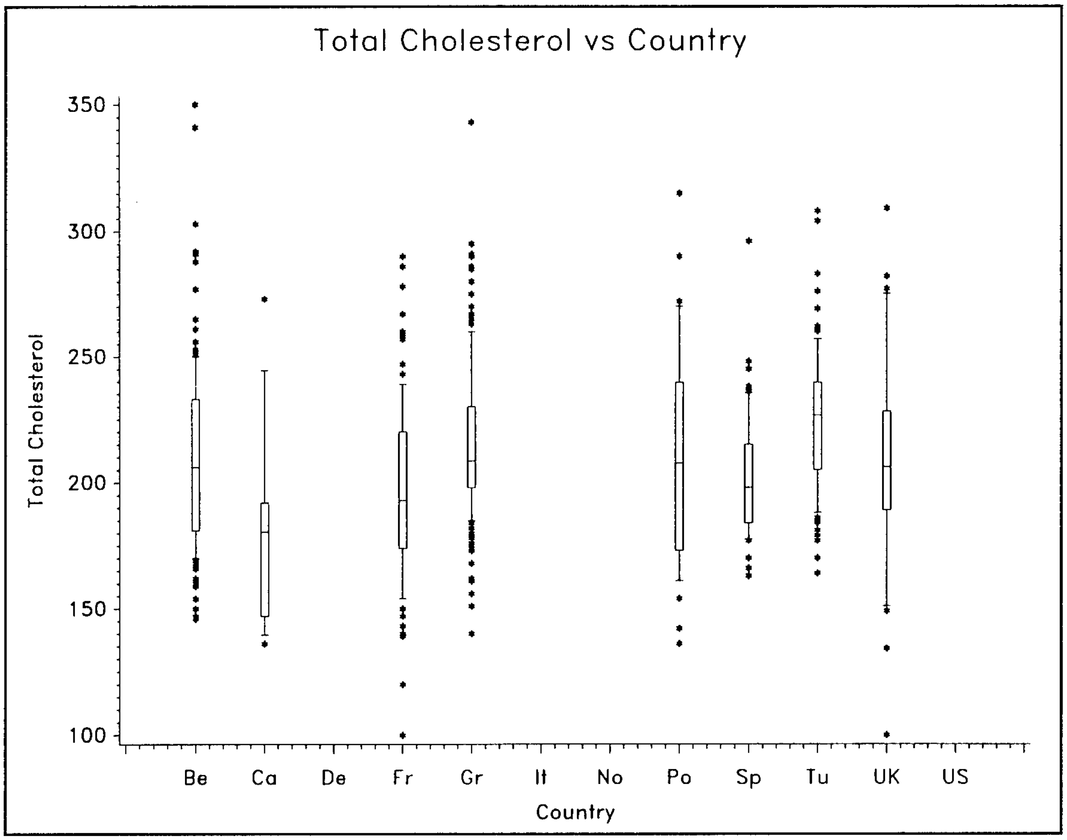
Next, the values of all echocardiographic measurements are presented in the same fashion by country and by XX versus ZZ pilots within each country. These graphs only present data for XX and ZZ pilots. As in the presentation of results earlier in this report, echocardiographic measurement data for other pilot subtypes is not displayed.

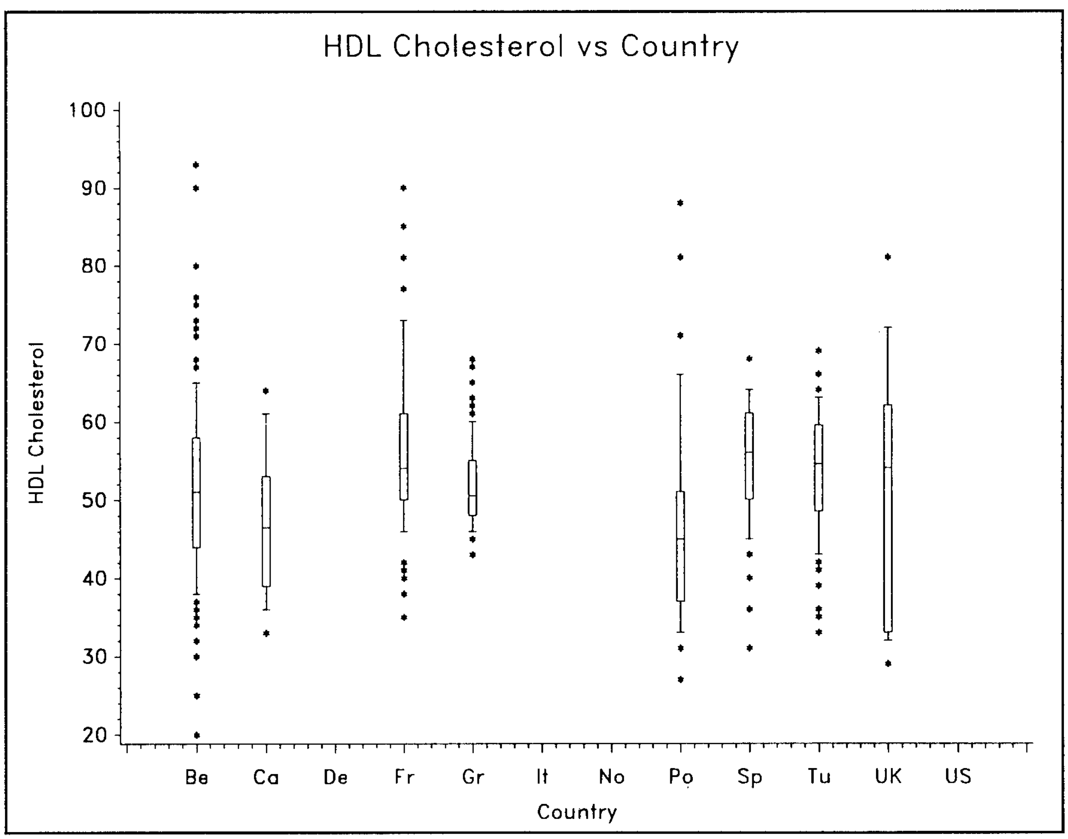

Age vs Country
Age
60
50
40
30
20
Be Ca De Fr Gr It No Po Sp Tu UK US
Country

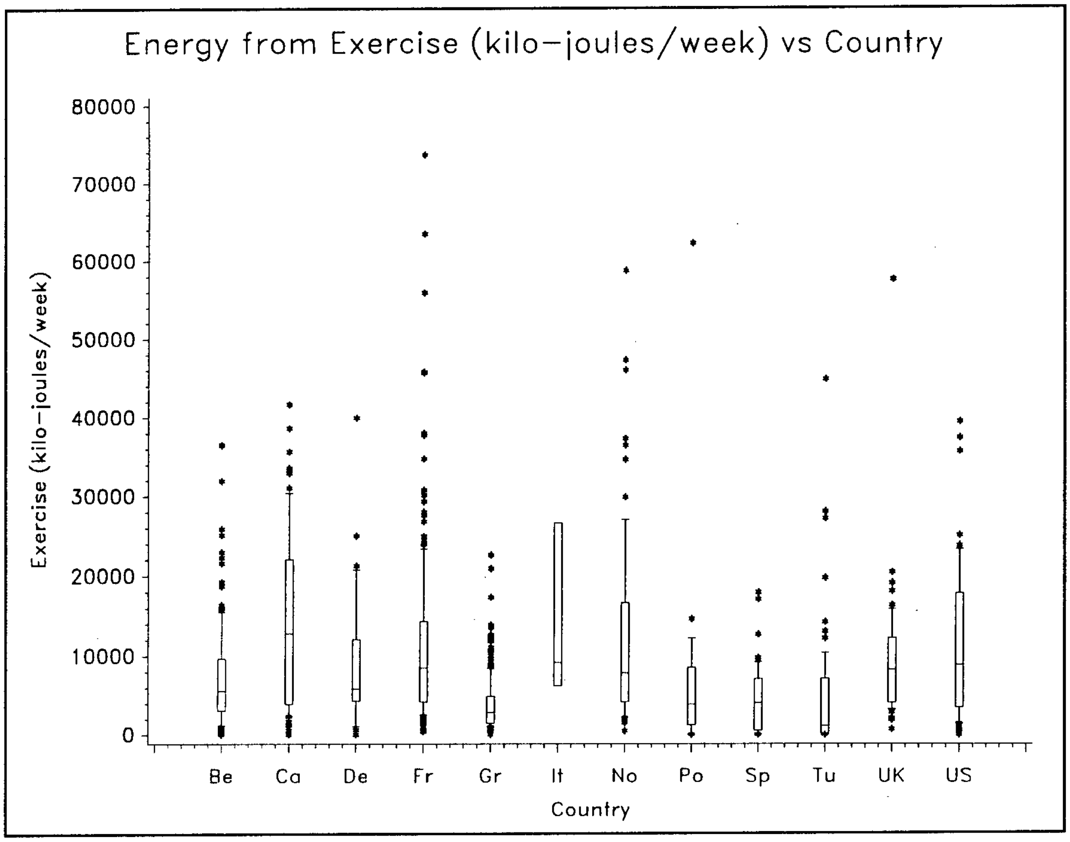

Body Surface Area vs Country
Body Surface Area
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
de Ca De Fr Gr It No Po Sp Tu UK US
Country

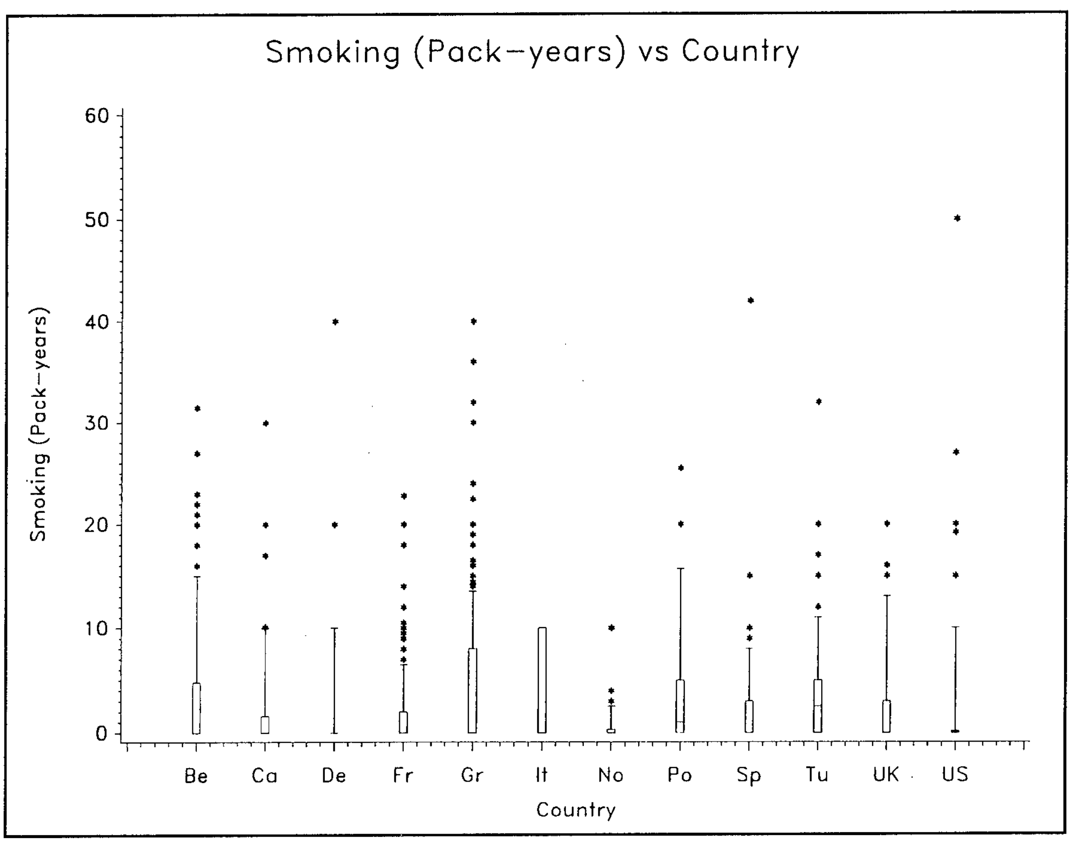

Systolic Blood Pressure (Seated) vs Country
Systolic BP – Seated
200
180
160
140
120
100
80
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

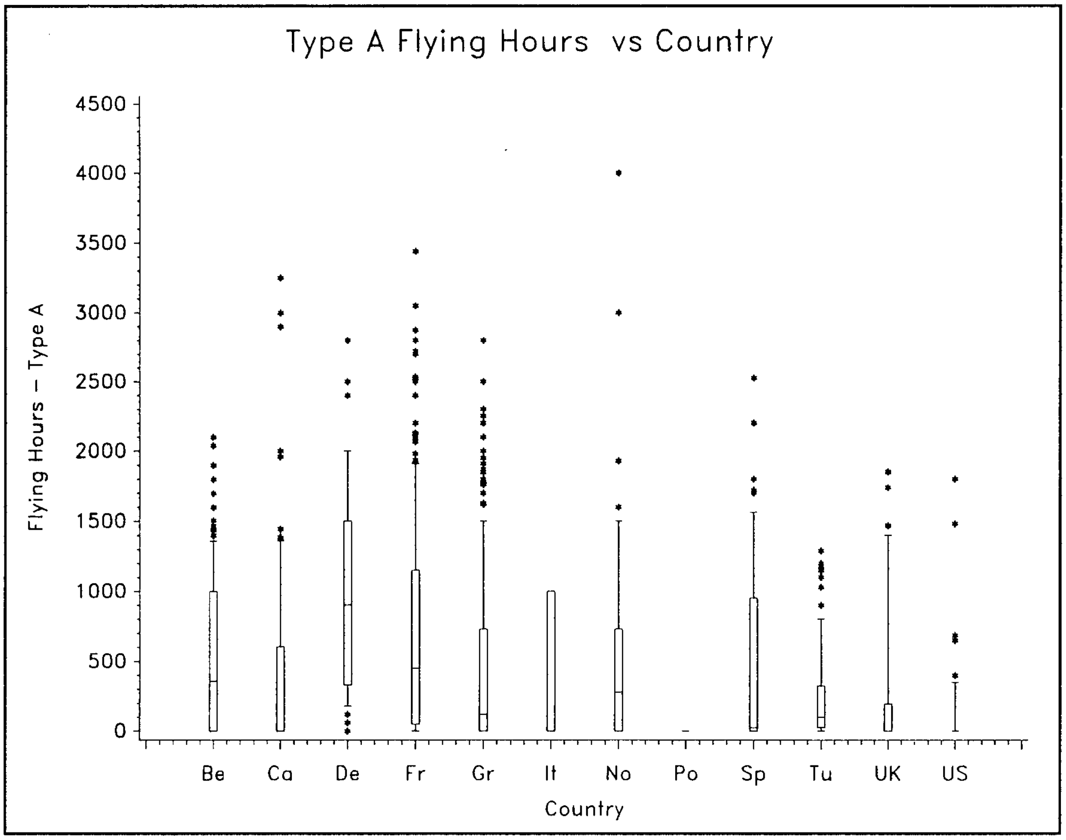

Diastolic Blood Pressure (Seated) vs Country
Diastolic BP – Seated
120
110
100
90
80
70
60
50
40
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

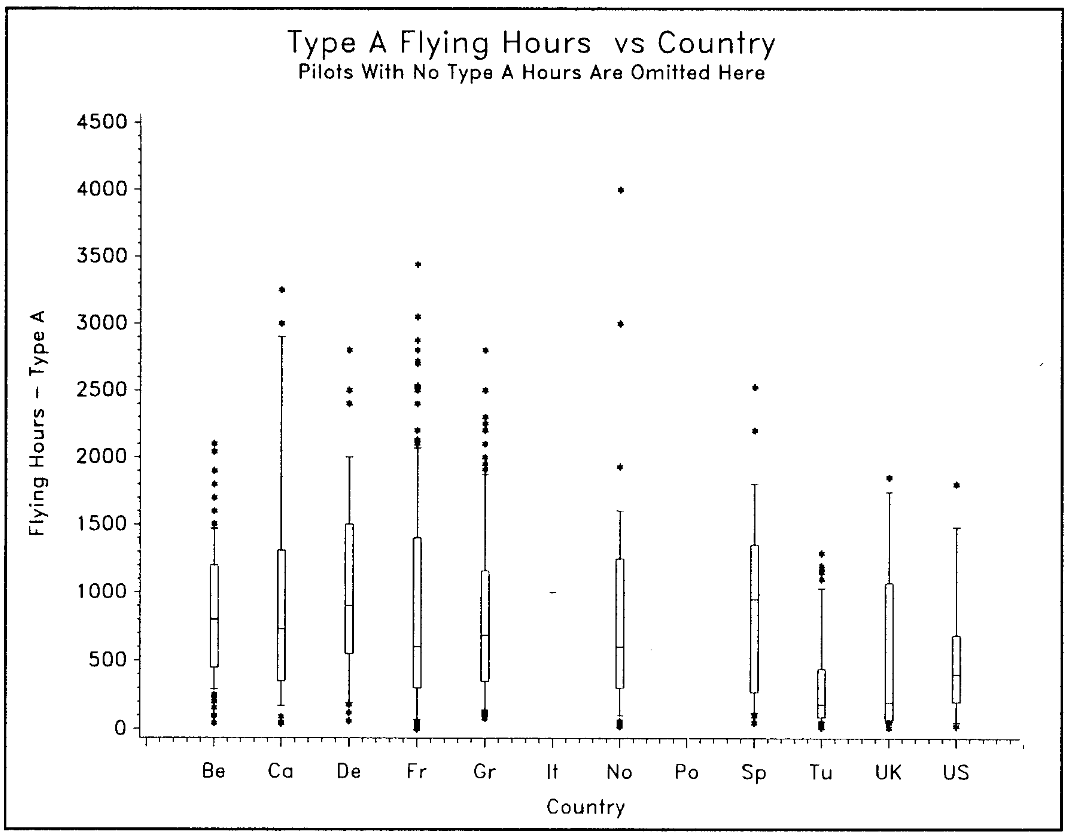

Total Cholesterol vs Country
Total Cholesterol
350
300
250
200
150
100
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

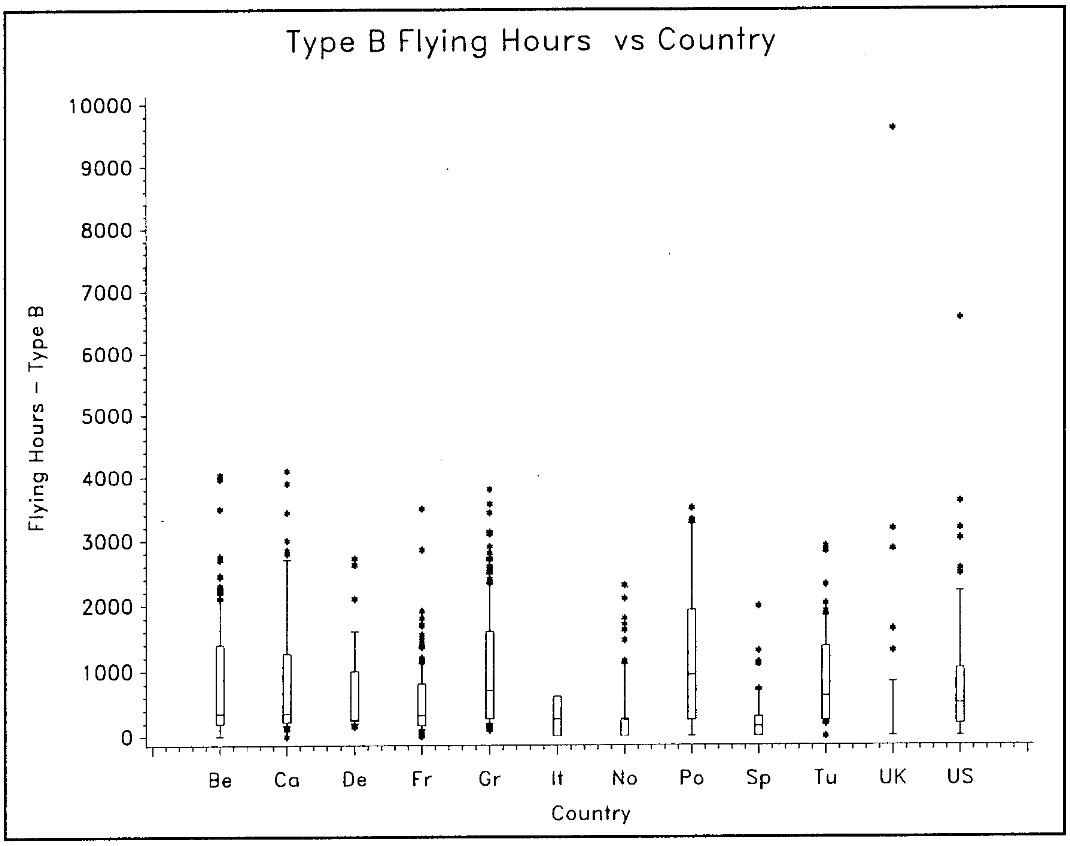

HDL Cholesterol vs Country
HDL Cholesterol
100
90
80
70
60
50
40
30
20
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

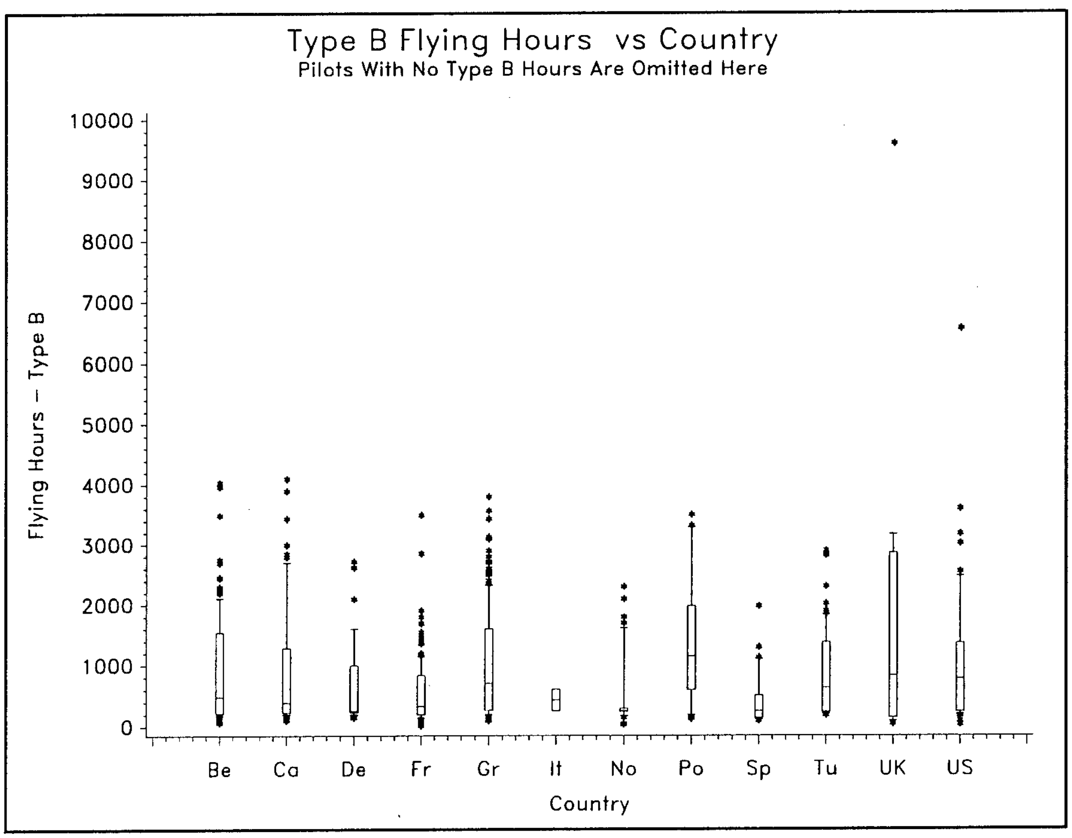

Energy from Exercise (kilo-joules/week) vs Country
Exercise (kilo-joules/week)
80000
70000
60000
50000
40000
30000
20000
10000
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

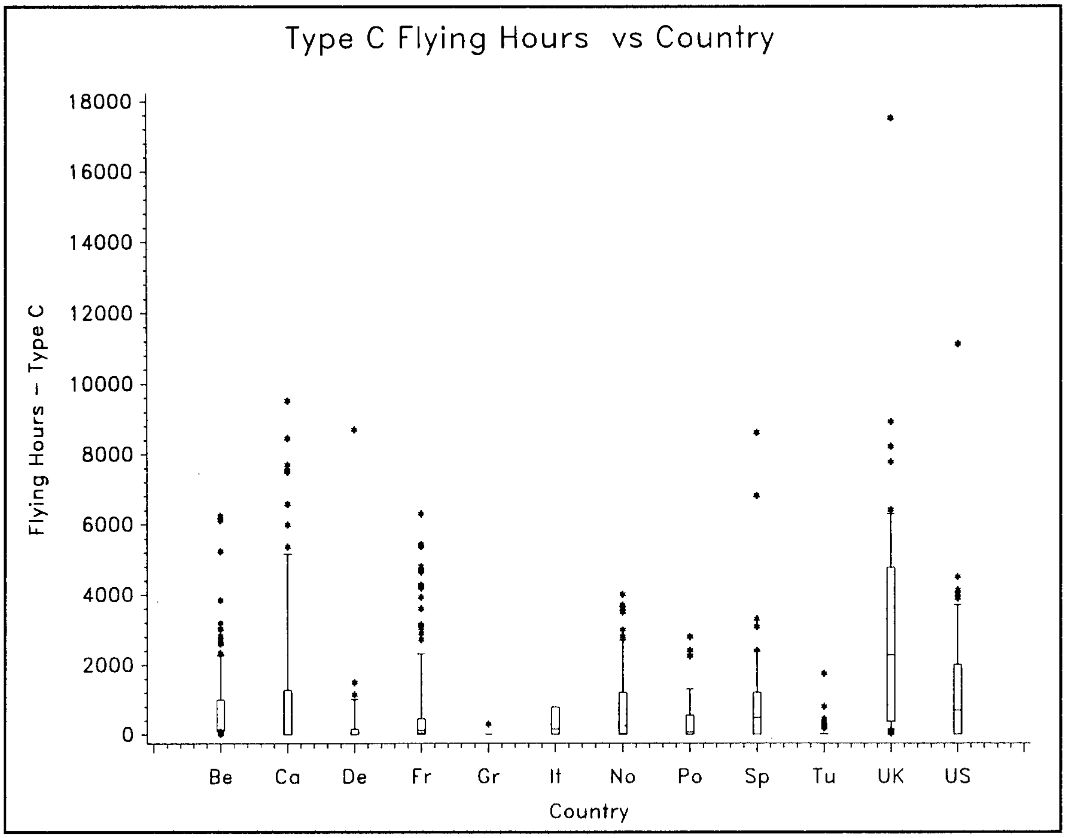

Smoking (Pack-years) vs Country
Smoking (Pack-years)
60
50
40
30
20
10
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

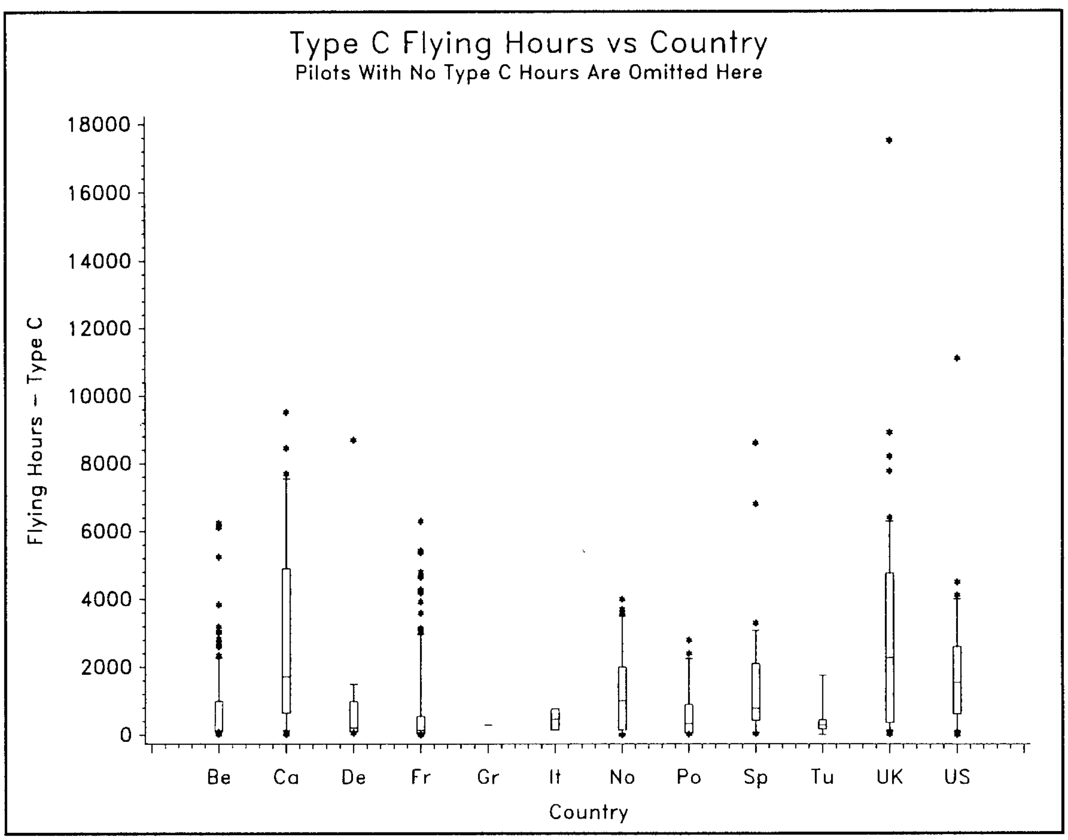

Type A Flying Hours vs Country
Flying Hours - Type A
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

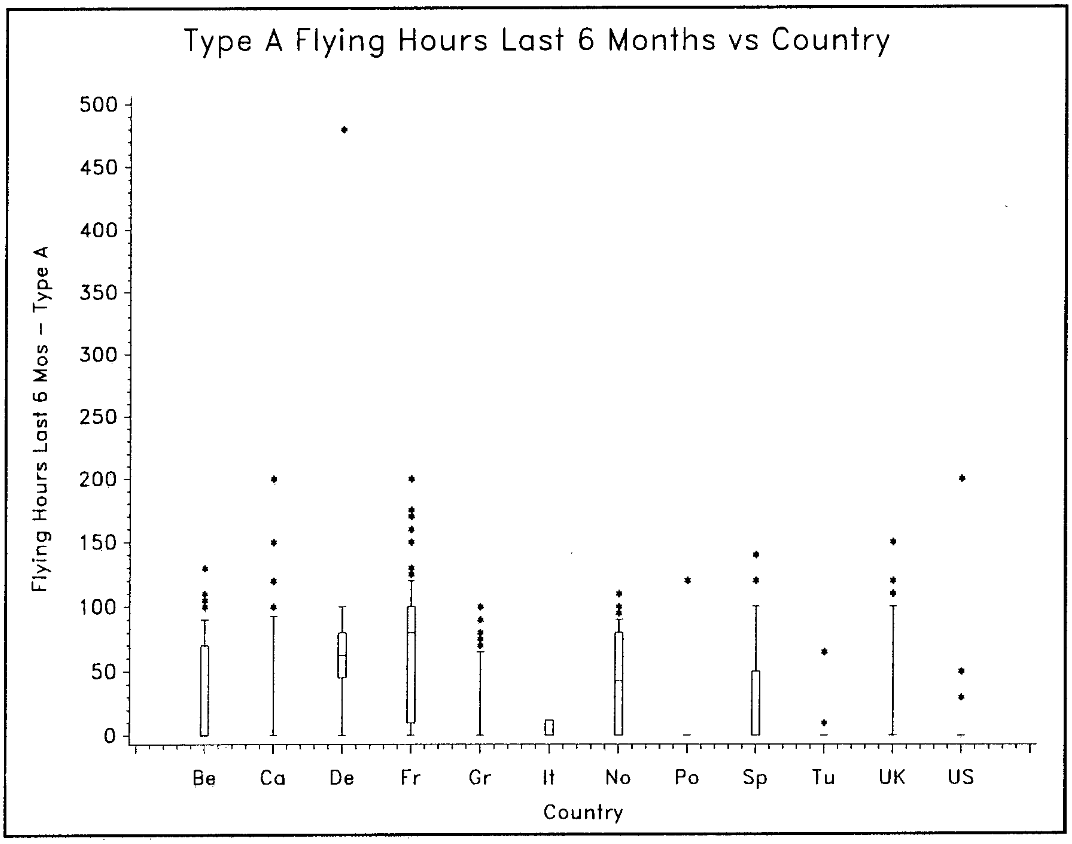

Type A Flying Hours vs Country
Pilots With No Type A Hours Are Omitted Here
Flying Hours - Type A
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

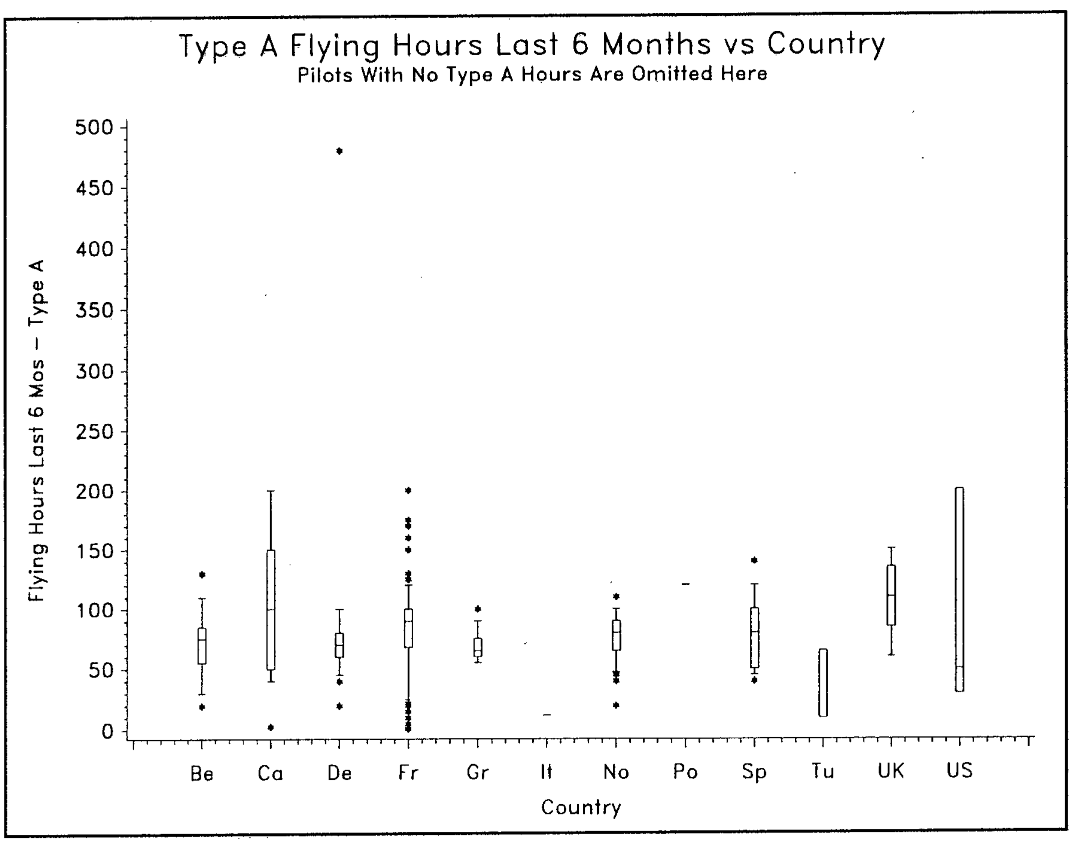

Type B Flying Hours vs Country
Flying Hours - Type B
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

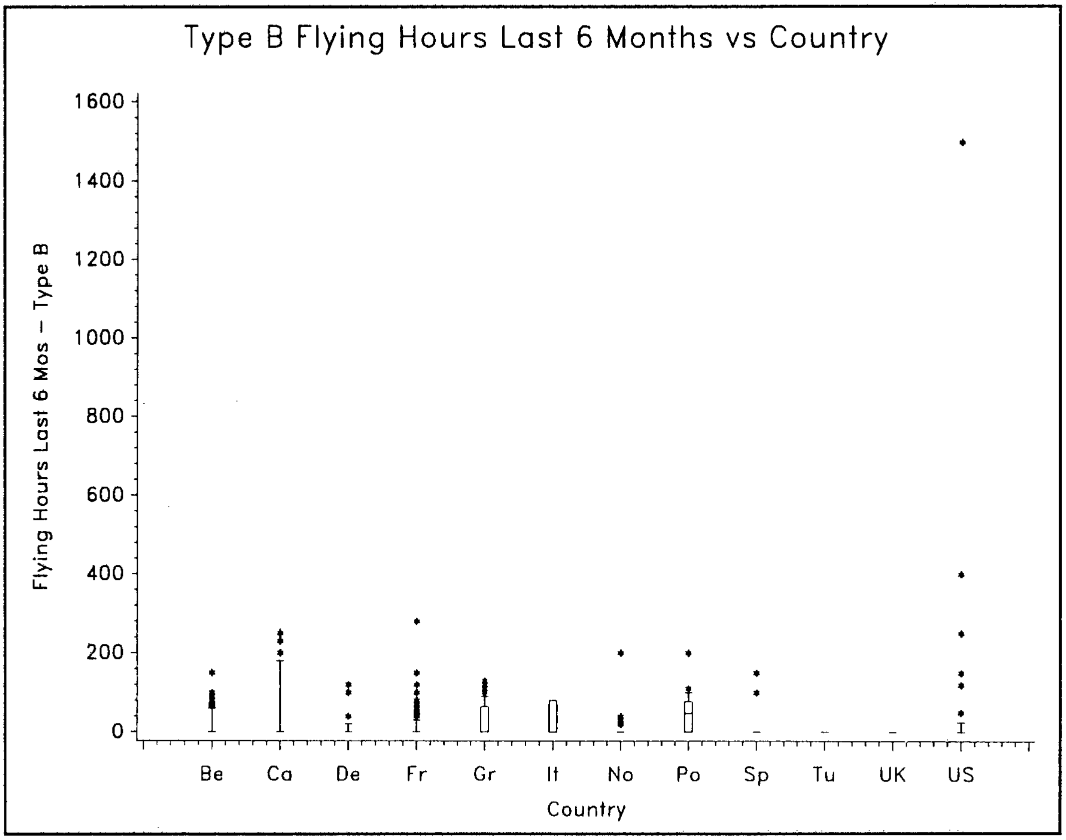

Type B Flying Hours vs Country
Pilots With No Type B Hours Are Omitted Here
Flying Hours - Type B
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

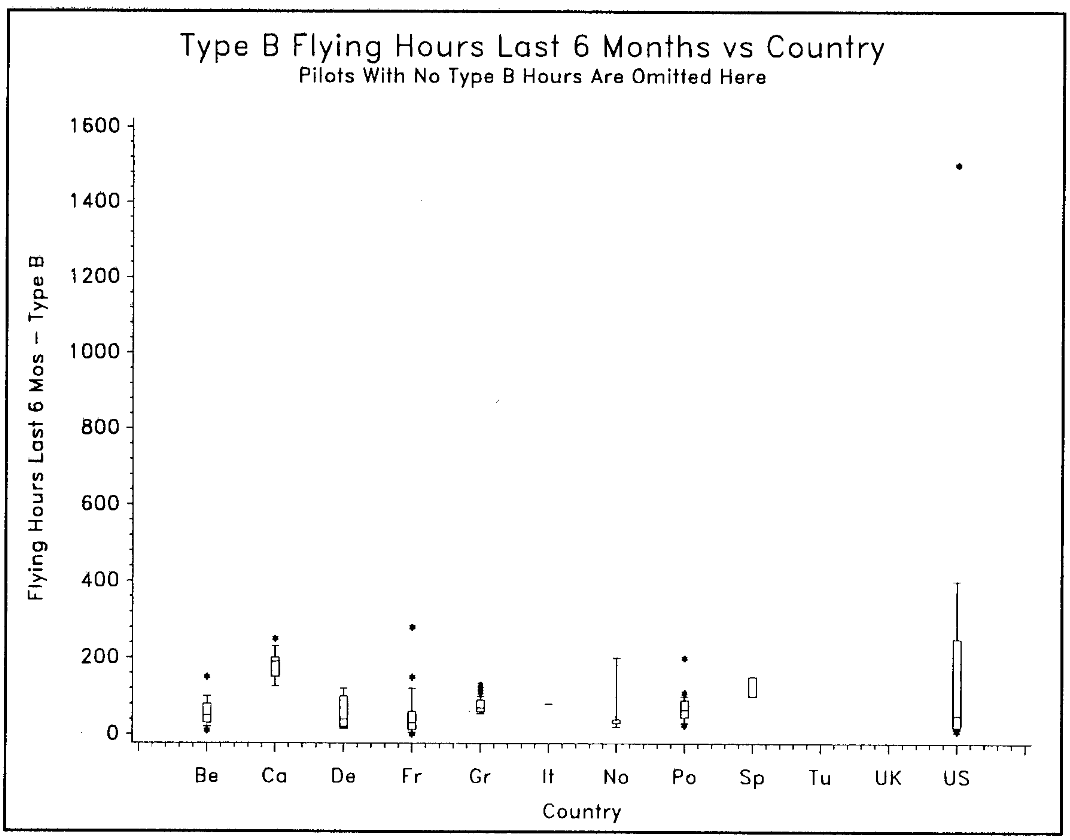

Type C Flying Hours vs Country
Flying Hours - Type C
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

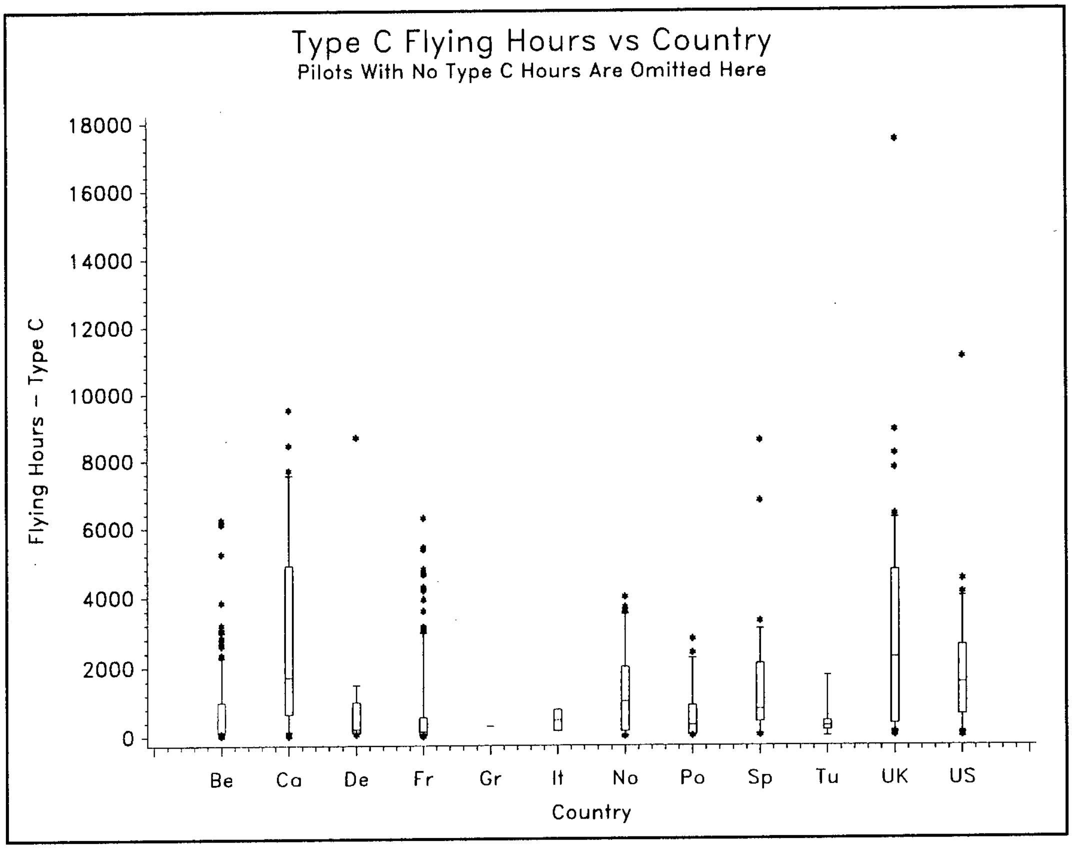

Type C Flying Hours vs Country
Pilots With No Type C Hours Are Omitted Here
Flying Hours - Type C
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

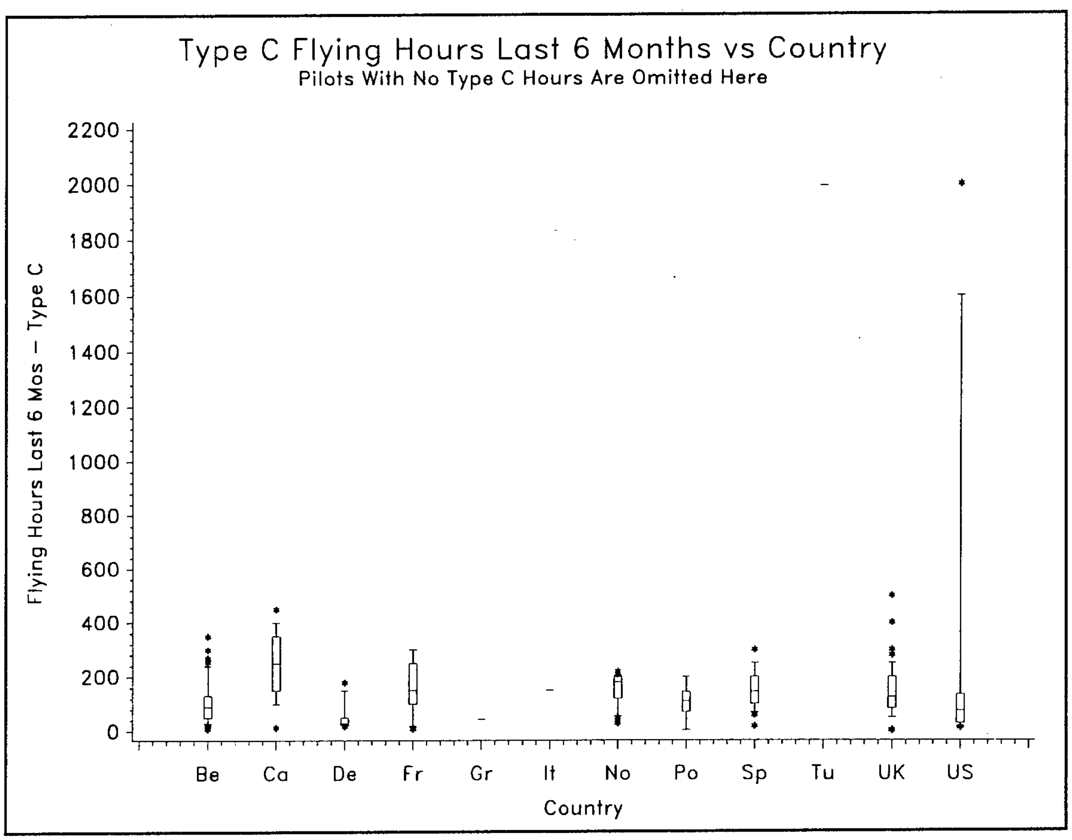

Type A Flying Hours Last 6 Months vs Country
Flying Hours Last 6 Mos – Type A
500
450
400
350
300
250
200
150
100
50
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

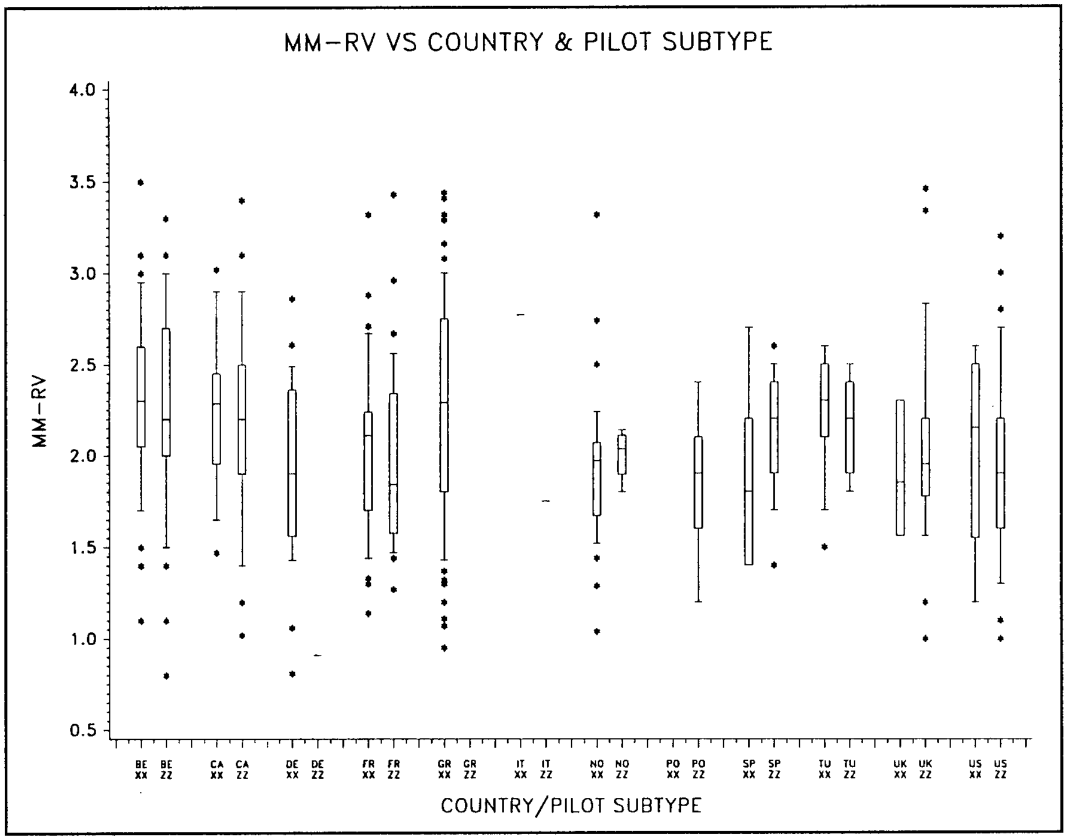

Type A Flying Hours Last 6 Months vs Country
Pilots With No Type A Hours Are Omitted Here
Flying Hours Last 6 Mos – Type A
500
450
400
350
300
250
200
150
100
50
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country

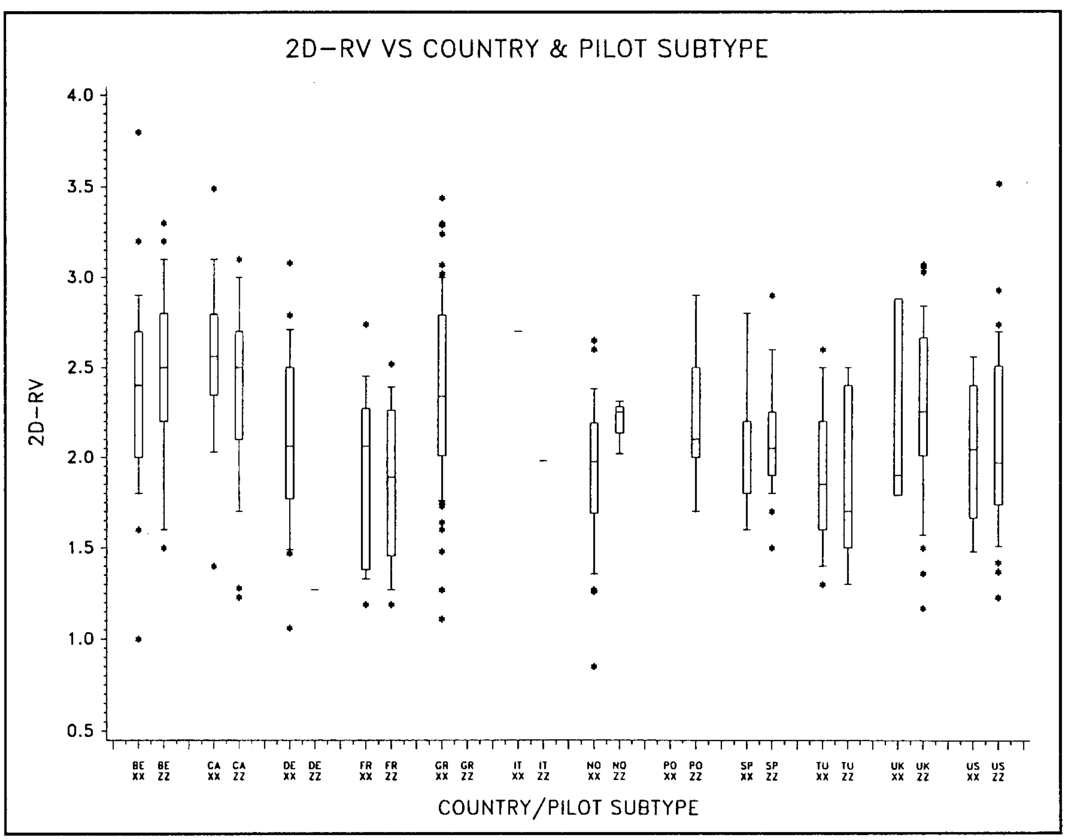

Type B Flying Hours Last 6 Months vs Country
Flying Hours Last 6 Mos - Type B
1600
1400
1200
1000
800
600
400
200
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country


Type B Flying Hours Last 6 Months vs Country
Pilots With No Type B Hours Are Omitted Here
Flying Hours Last 6 Mos - Type B
1600
1400
1200
1000
800
600
400
200
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country


Type C Flying Hours vs Country
Pilots With No Type C Hours Are Omitted Here
Flying Hours - Type C
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country


Type C Flying Hours Last 6 Months vs Country
Pilots With No Type C Hours Are Omitted Here
Flying Hours Last 6 Mos - Type C
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Be
Ca
De
Fr
Gr
It
No
Po
Sp
Tu
UK
US
Country


MM-RV VS COUNTRY & PILOT SUBTYPE
MM-RV
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
BE XX
BE ZZ
CA XX
CA ZZ
DE XX
DE ZZ
FR XX
FR ZZ
GR XX
GR ZZ
IT XX
IT ZZ
NO XX
NO ZZ
PO XX
PO ZZ
SP XX
SP ZZ
TU XX
TU ZZ
UK XX
UK ZZ
US XX
US ZZ
COUNTRY/PILOT SUBTYPE


2D-RV VS COUNTRY & PILOT SUBTYPE
2D-RV
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
BE XX
BE ZZ
CA XX
CA ZZ
DE XX
DE ZZ
FR XX
FR ZZ
GR XX
GR ZZ
IT XX
IT ZZ
NO XX
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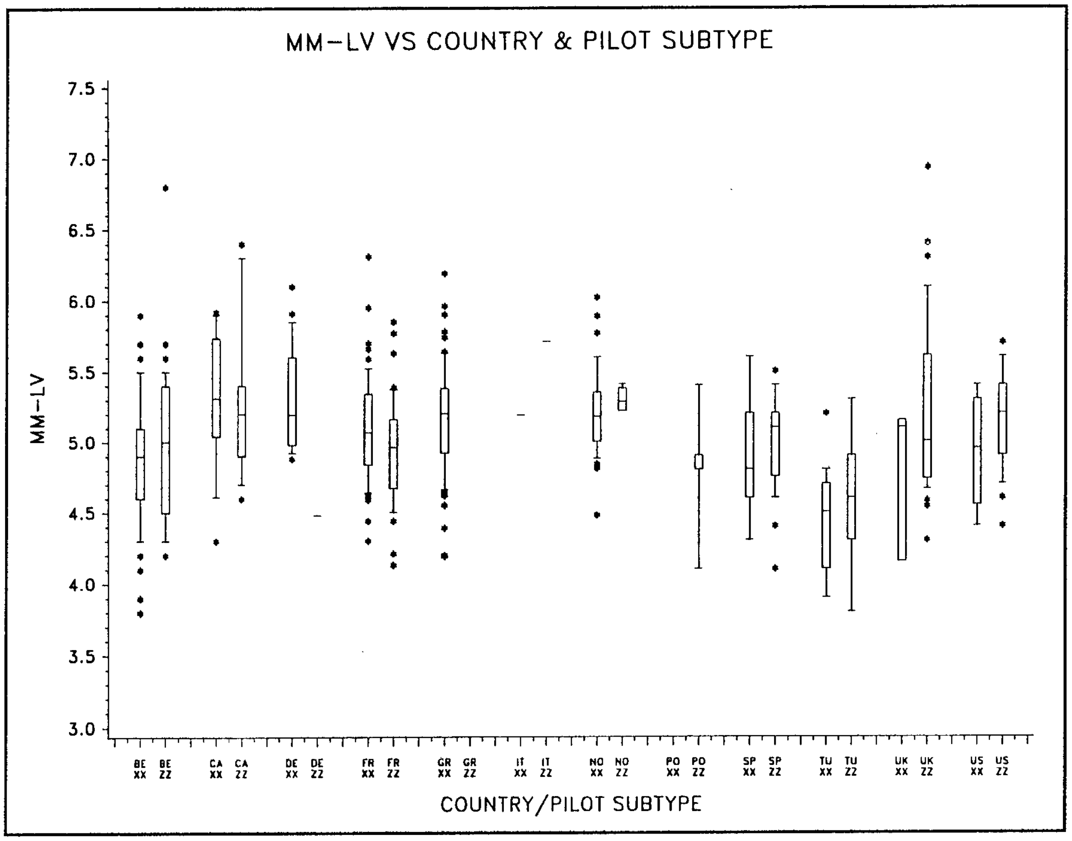
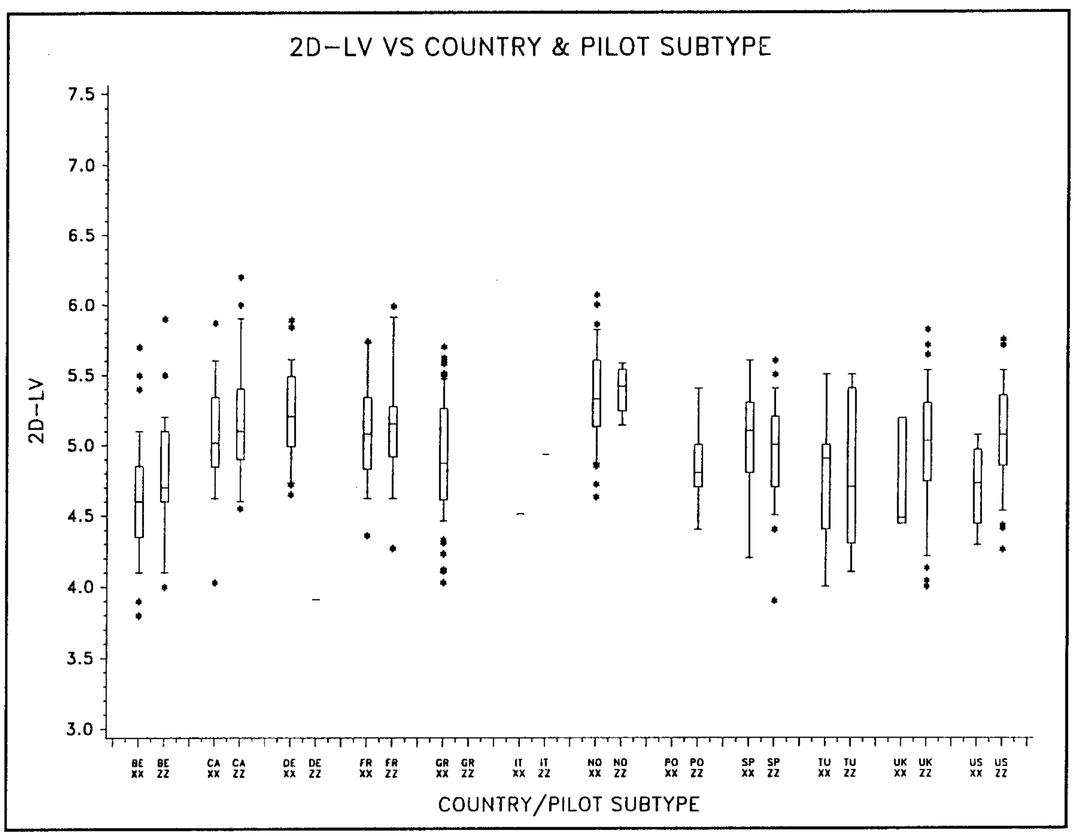
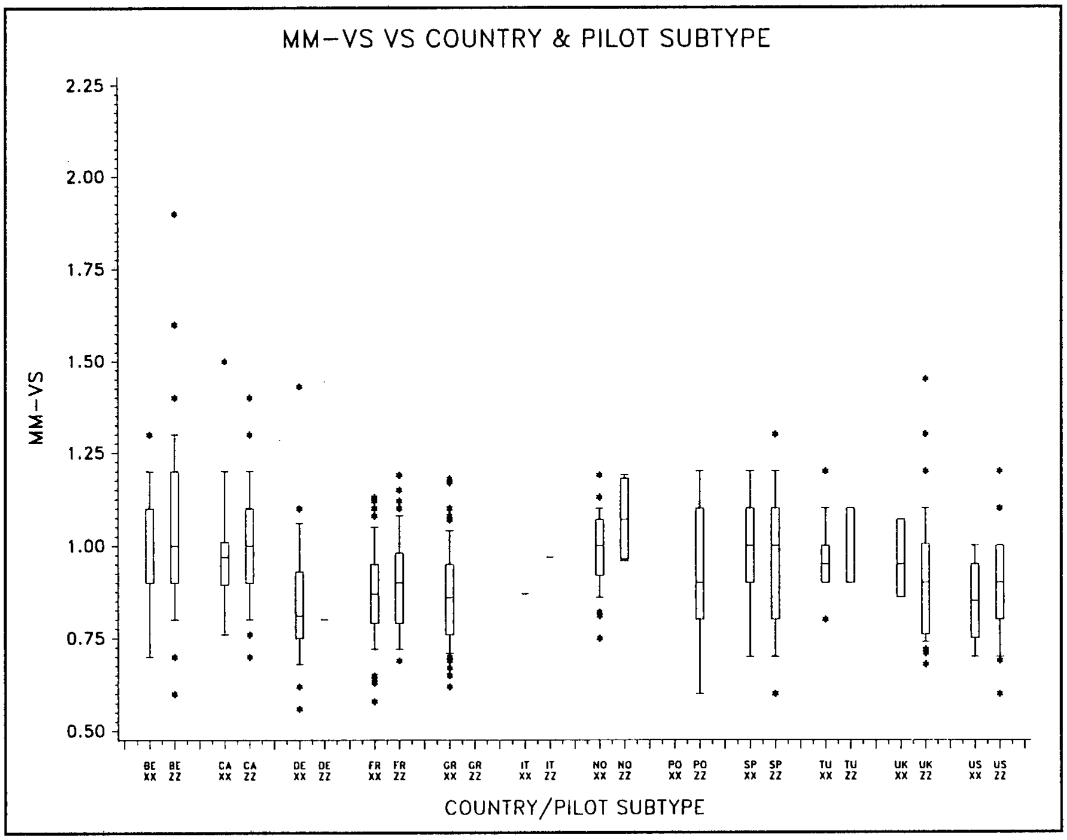
US ZZ
COUNTRY/PILOT SUBTYPE


MM–LV VS COUNTRY & PILOT SUBTYPE
MM–LV
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
BE XX BE ZZ CA XX CA ZZ DE XX DE ZZ FR XX FR ZZ GR XX GR ZZ IT XX IT ZZ NO XX NO ZZ PO XX PO ZZ SP XX SP ZZ TU XX TU ZZ UK XX UK ZZ US XX US ZZ
COUNTRY/PILOT SUBTYPE


2D–LV VS COUNTRY & PILOT SUBTYPE
2D–LV
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
BE XX BE ZZ CA XX CA ZZ DE XX DE ZZ FR XX FR ZZ GR XX GR ZZ IT XX IT ZZ NO XX NO ZZ PO XX PO ZZ SP XX SP ZZ TU XX TU ZZ UK XX UK ZZ US XX US ZZ
COUNTRY/PILOT SUBTYPE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MM-VS
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
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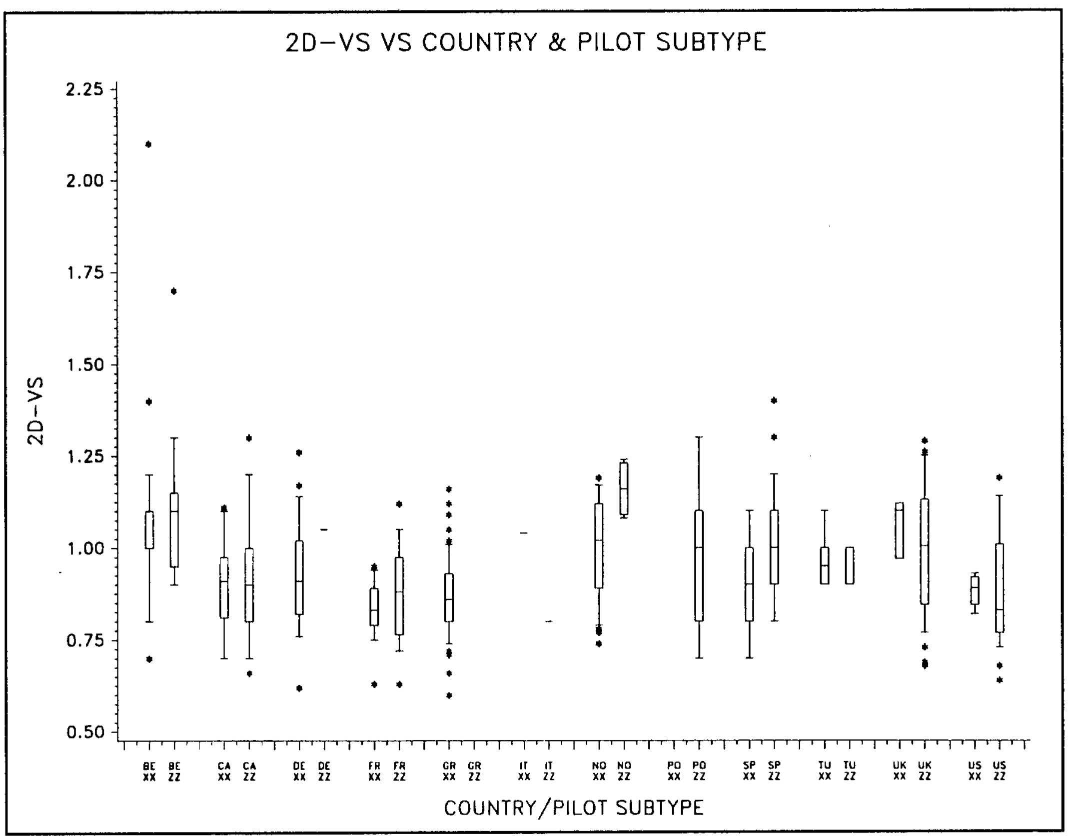
2D-VS VS COUNTRY & PILOT SUBTYPE
2D-VS
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
BE XX BE ZZ CA XX CA ZZ DE XX DE ZZ FR XX FR ZZ GR XX GR ZZ IT XX IT ZZ NO XX NO ZZ PO XX PO ZZ SP XX SP ZZ TU XX TU ZZ UK XX UK ZZ US XX US ZZ
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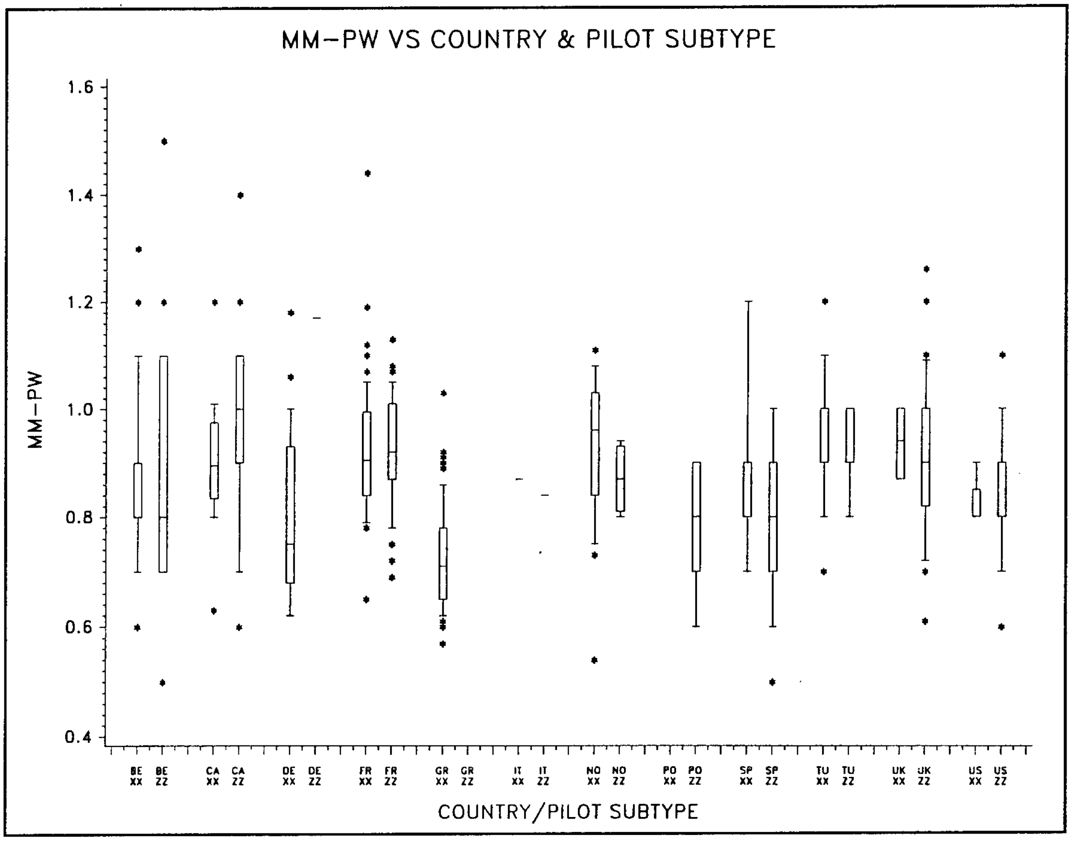
MM–PW VS COUNTRY & PILOT SUBTYPE
MM–PW
1.6
1.4
1.2
1.0
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0.6
0.4
BE XX
BE ZZ
CA XX
CA ZZ
DE XX
DE ZZ
FR XX
FR ZZ
GR XX
GR ZZ
IT XX
IT ZZ
NO XX
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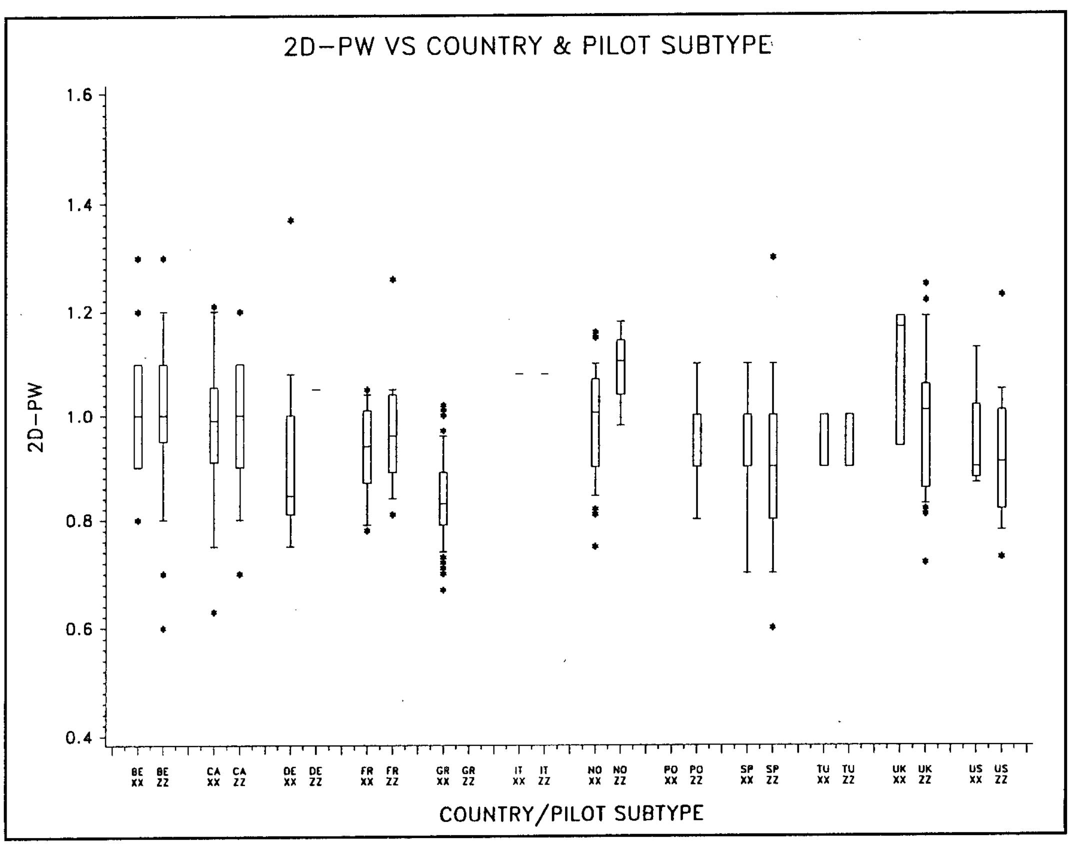
US XX
US ZZ
COUNTRY/PILOT SUBTYPE


2D–PW VS COUNTRY & PILOT SUBTYPE
2D–PW
1.6
1.4
1.2
1.0
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0.6
0.4
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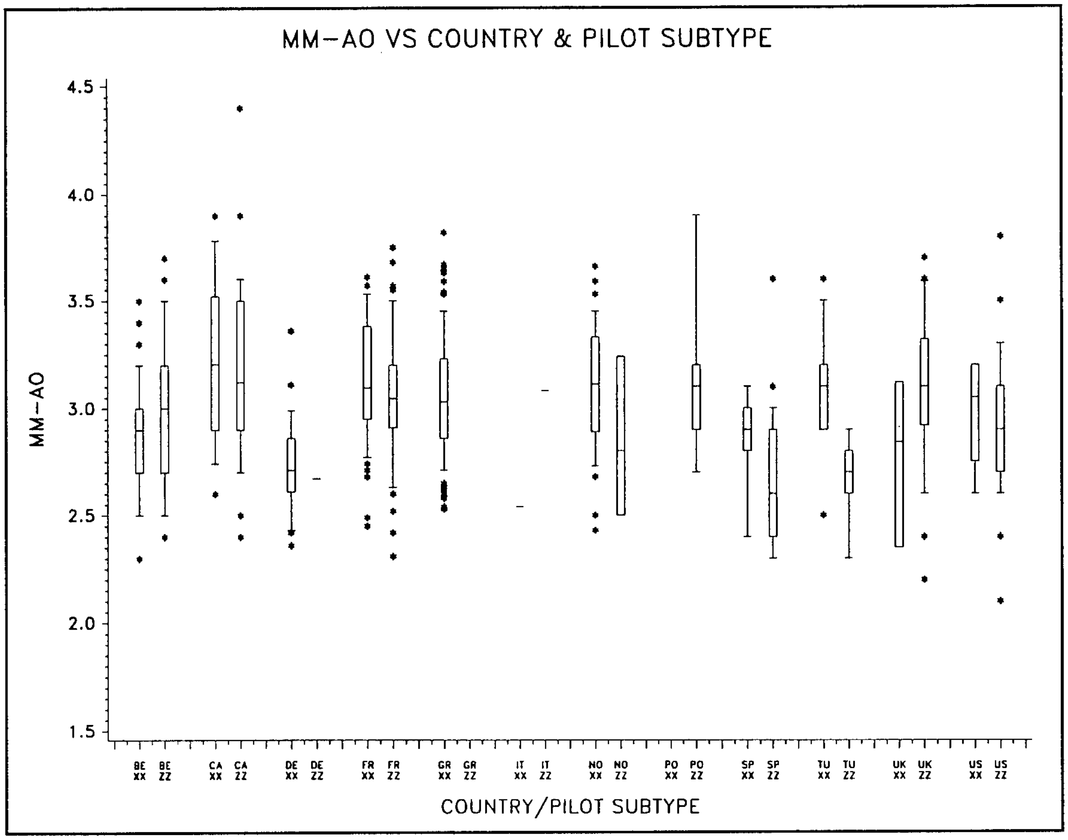
MM–AO VS COUNTRY & PILOT SUBTYPE
MM–AO
4.5
4.0
3.5
3.0
2.5
2.0
1.5
BE XX BE ZZ CA XX CA ZZ DE XX DE ZZ FR XX FR ZZ GR XX GR ZZ IT XX IT ZZ NO XX NO ZZ PO XX PO ZZ SP XX SP ZZ TU XX TU ZZ UK XX UK ZZ US XX US ZZ
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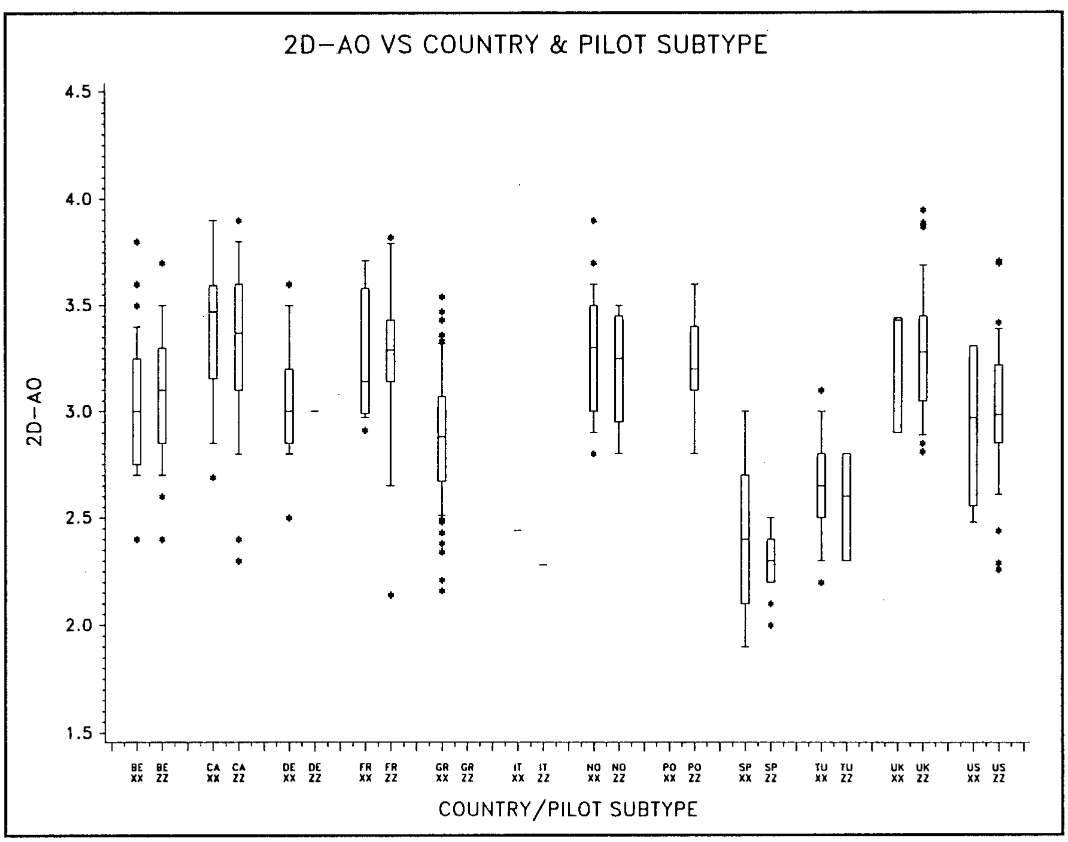
2D–AO VS COUNTRY & PILOT SUBTYPE
2D–AO
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4.0
3.5
3.0
2.5
2.0
1.5
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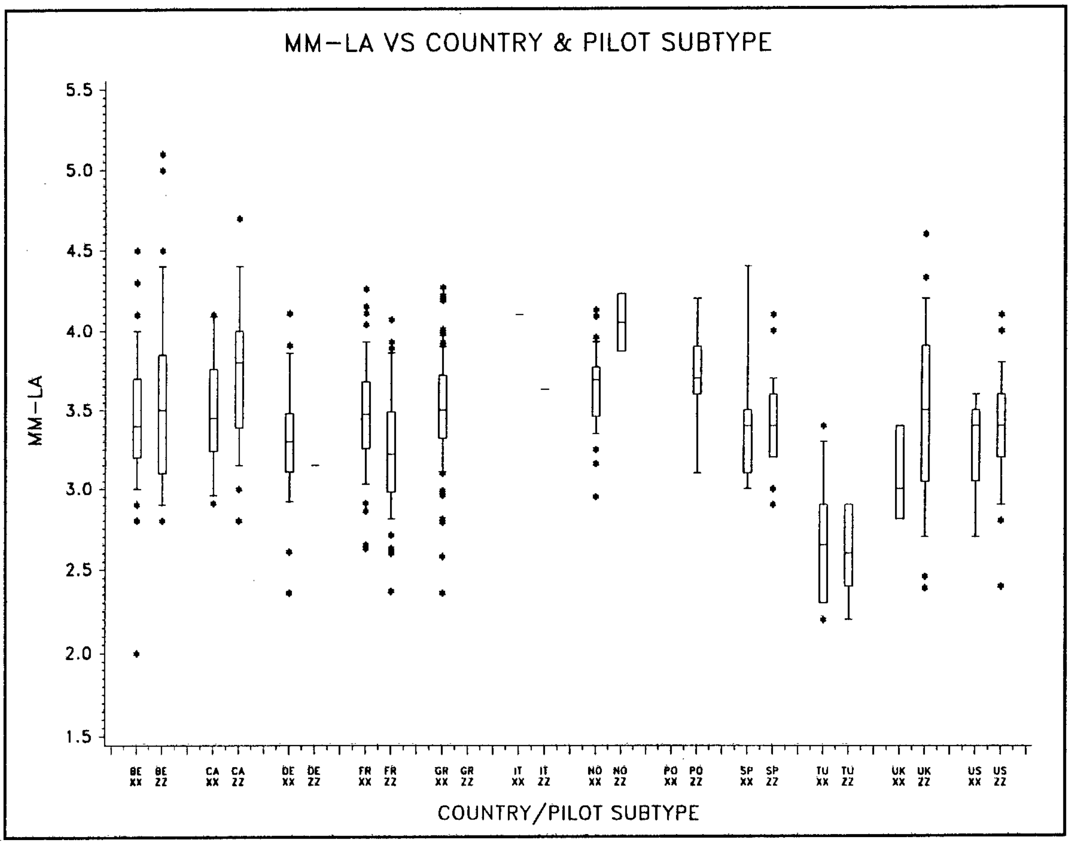
MM-LA VS COUNTRY & PILOT SUBTYPE
MM-LA
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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BE ZZ
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CA ZZ
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DE ZZ
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GR ZZ
IT XX
IT ZZ
NO XX
NO ZZ
PO XX
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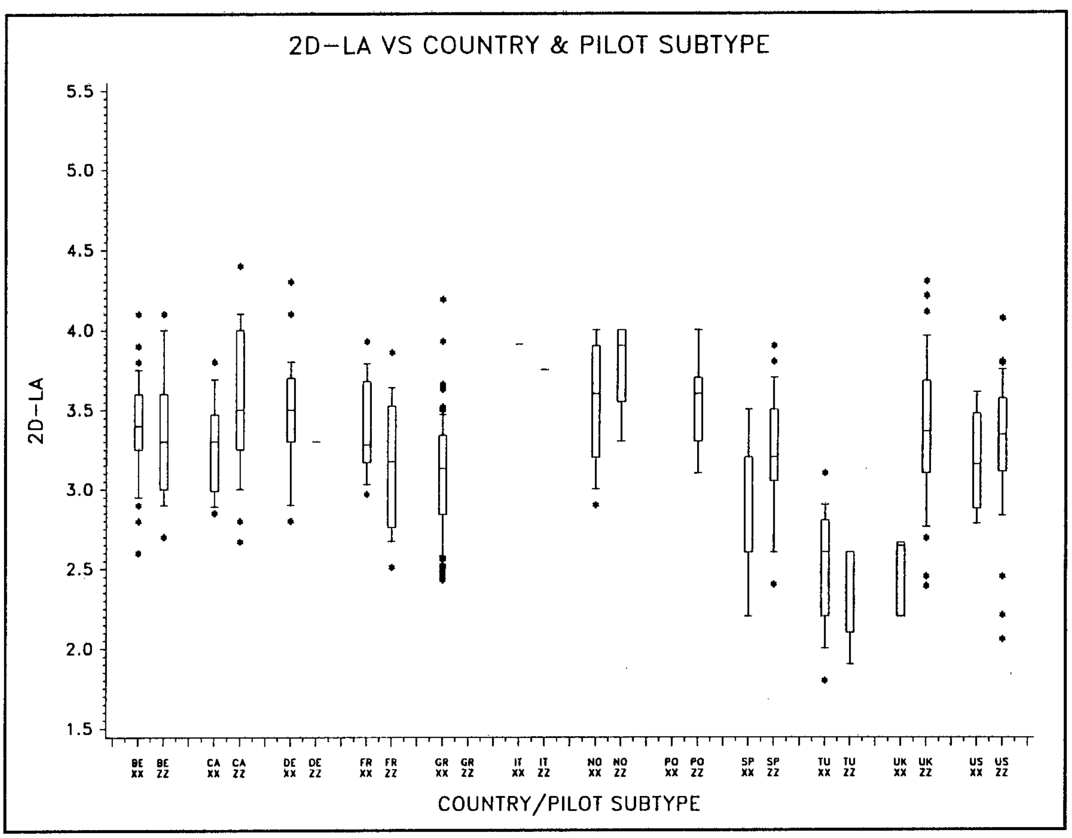
US ZZ
COUNTRY/PILOT SUBTYPE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4.0
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3.0
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DE ZZ
FR XX
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GR XX
GR ZZ
IT XX
IT ZZ
NO XX
NO ZZ
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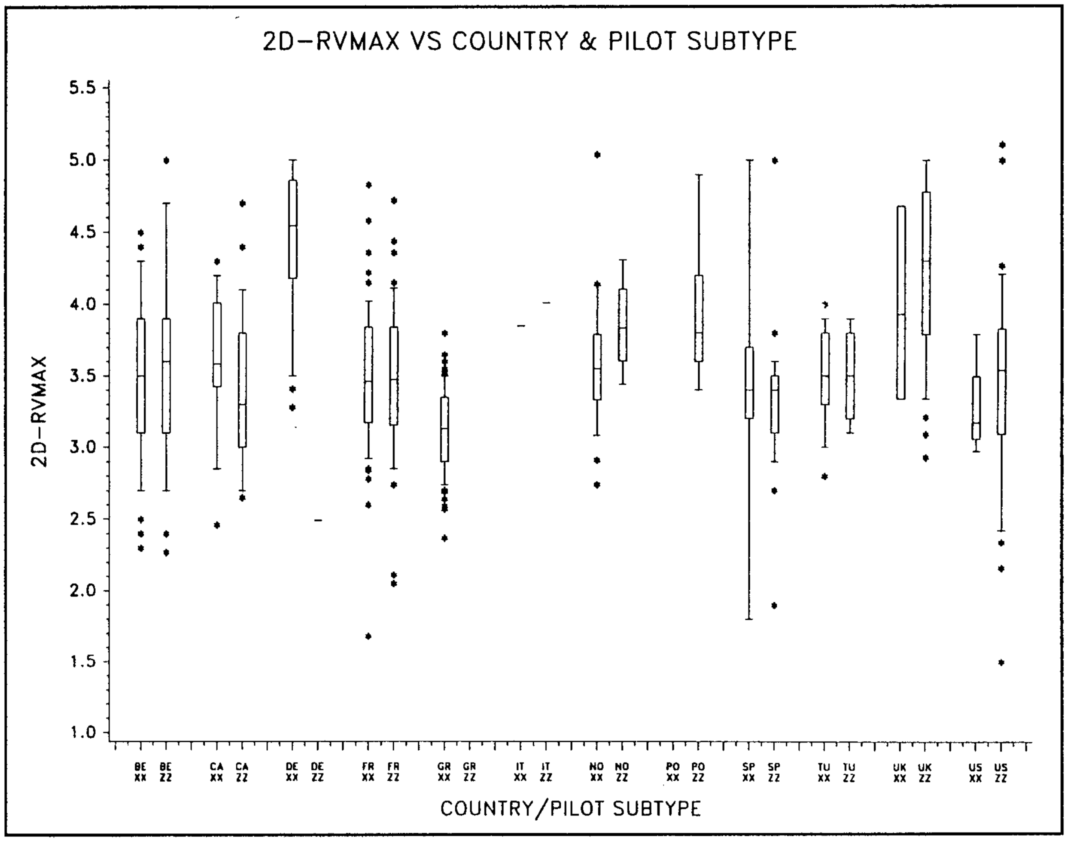
US ZZ
COUNTRY/PILOT SUBTYPE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2D-RVMAX
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
BE XX
BE ZZ
CA XX
CA ZZ
DE XX
DE ZZ
FR XX
FR ZZ
GR XX
GR ZZ
IT XX
IT ZZ
NO XX
NO ZZ
PO XX
PO ZZ
SP XX
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TU ZZ
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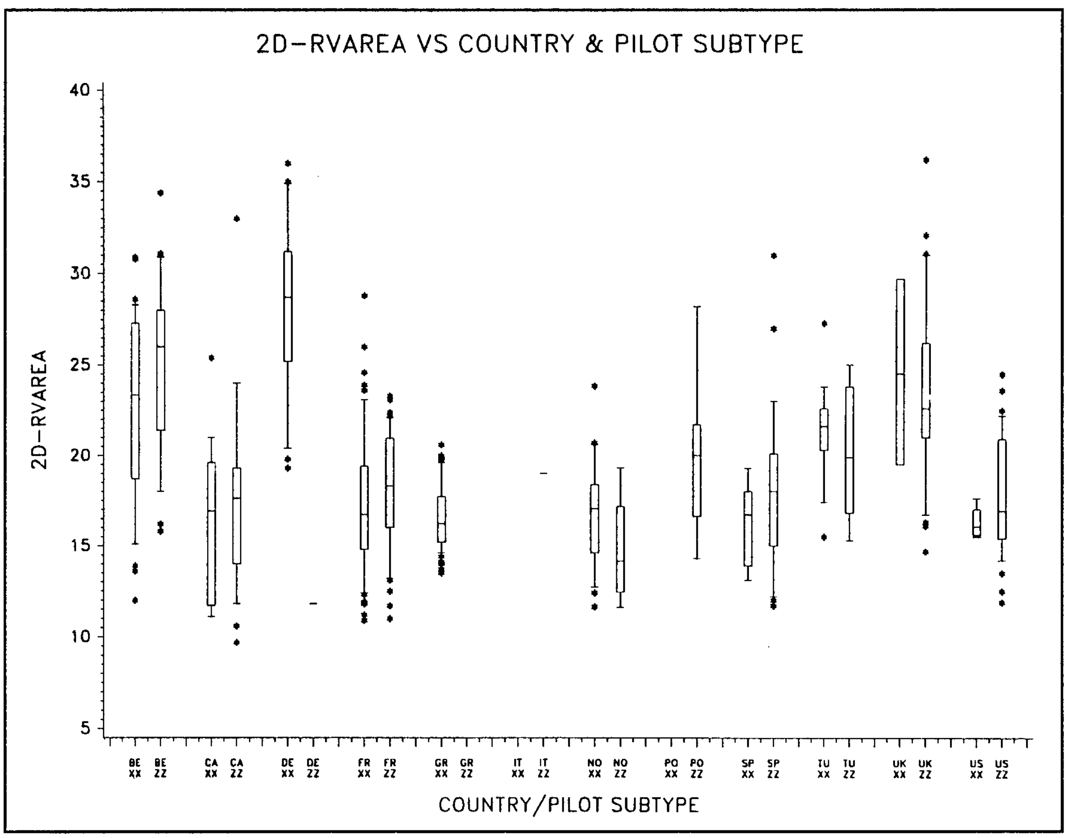
US ZZ
COUNTRY/PILOT SUBTYPE


2D-RVAREA VS COUNTRY & PILOT SUBTYPE
2D-RVAREA
40
35
30
25
20
15
10
5
BE XX
BE ZZ
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CA ZZ
DE XX
DE ZZ
FR XX
FR ZZ
GR XX
GR ZZ
IT XX
IT ZZ
NO XX
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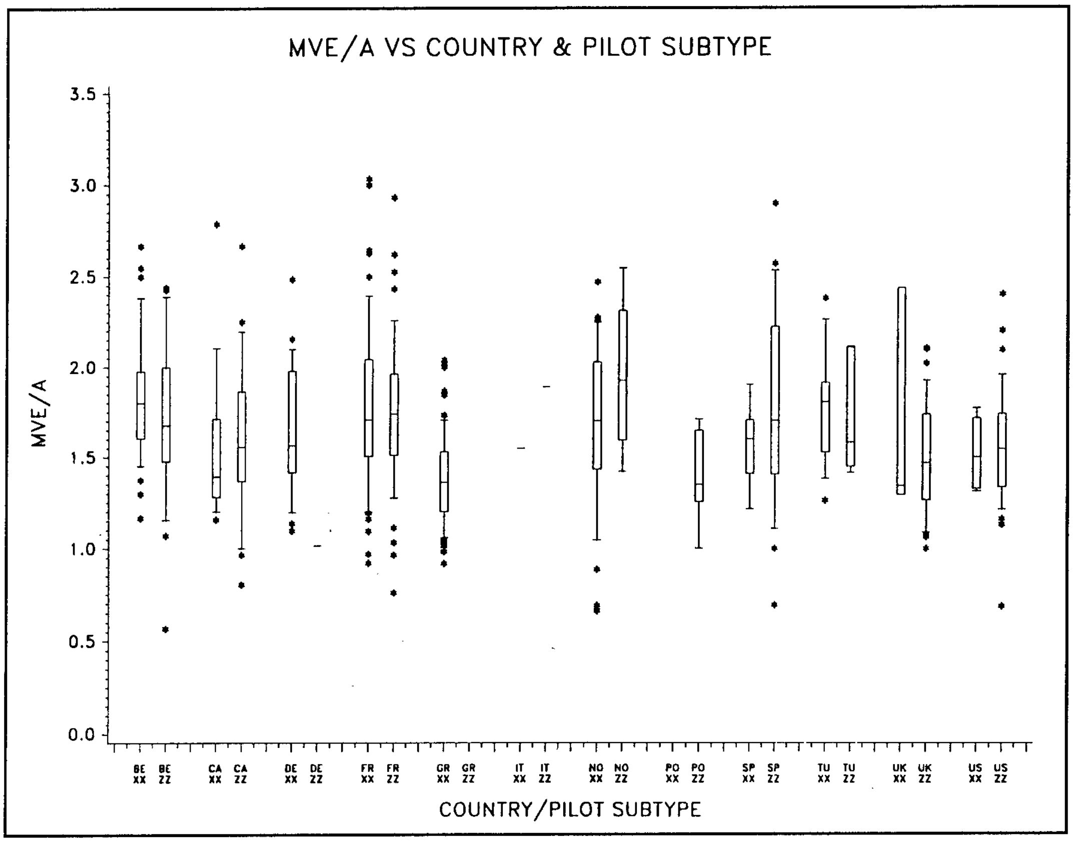
US XX
US ZZ
COUNTRY/PILOT SUBTYPE


MVE/A VS COUNTRY & PILOT SUBTYPE
MVE/A
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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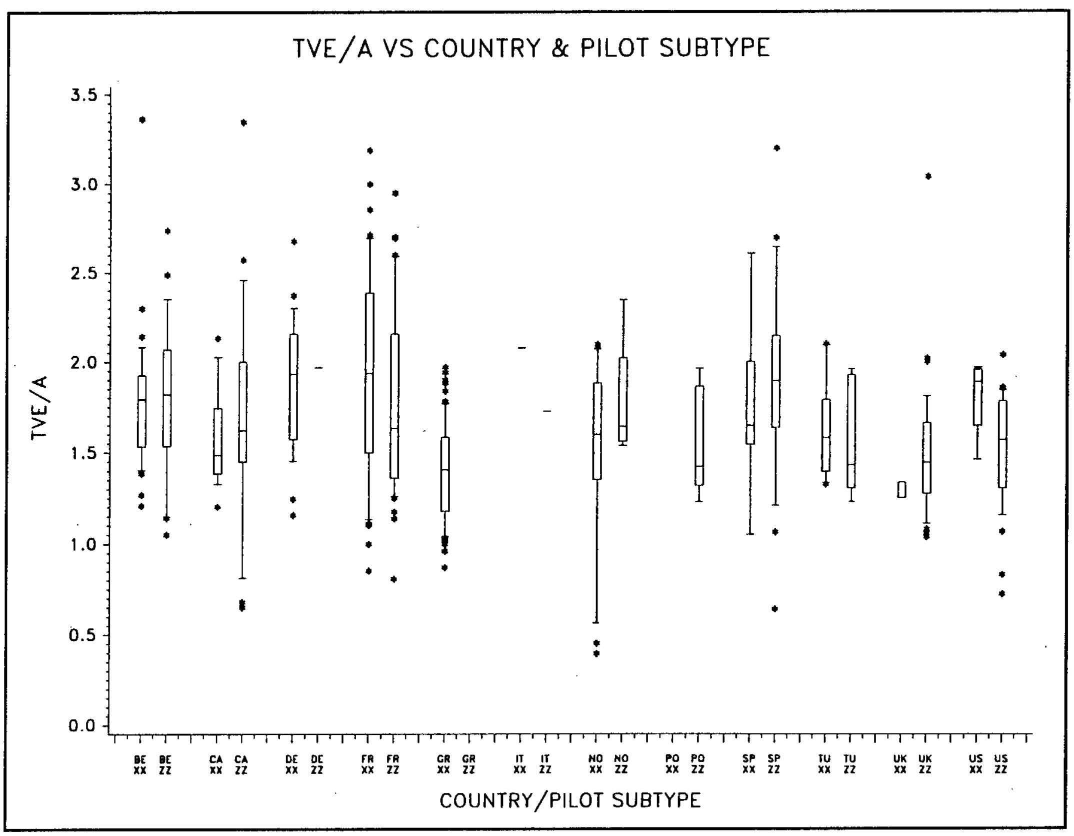
TVE/A VS COUNTRY & PILOT SUBTYPE
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2.5
2.0
1.5
1.0
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BE XX BE ZZ CA XX CA ZZ DE XX DE ZZ FR XX FR ZZ GR XX GR ZZ IT XX IT ZZ NO XX NO ZZ PO XX PO ZZ SP XX SP ZZ TU XX TU ZZ UK XX UK ZZ US XX US ZZ
COUNTRY/PILOT SUBTYPE

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Tolerances (physioogy)	Gravity
Fighter aircraft	Ultrasonic tests
Aerospace medicine	Protocols

14. Abstract

This report addresses the results of an AGARD epidemiological study of NATO aircrew, utilizing echocardiographic studies. This echocardiographic project was performed by AGARD Working Group 18, based upon an extensive protocol written by Working Group 13. The goal of the study was to determine whether repeated high sustained +Gz acceleration produced permanent structural or functional changes in the heart, when compared to a control group of non-high performance pilots. The results conclusively confirm the absence of any abnormal echocardiographic parameters in the high sustained G pilots.

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